REFERENCE ONLY

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N-Heterocyclic carbenes and their application as ligands for transition metal mediated synthesis

A Thesis Presented by

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Abstract

The present thesis describes a range of studies on the generation and application of *N*-heterocyclic carbene species capable of acting as ligands to a variety of transition metals. These novel complexes are then applied to a variety of common organic transformations.

This thesis opens with two distinct introductory reviews. The first focuses on recent developments on the generation and application of *N*-heterocyclic carbenes as ligands. The second is concerned with the specific area of hydrogen transfer reactions.

The results and discussion section firstly describes the successful generation of free 'pincer' type carbene moieties, their complexation with ruthenium and the application of these new catalysts to oxidation/reduction reactions. This new organometallic complexes are found to undergo hydrogen transfer reactions with a range of substrates (alcohol/carbonyl based) under a variety of conditions to yield the corresponding product (alcohol/carbonyl based). Subsequent studies are directed towards novel syntheses of the parent carbene precursor, the free carbene or the carbene-transition metal complex are then discussed.

Preparation of a 'second generation' acac based ligands will be presented in the penultimate results and discussion section of the thesis. From this study, an array of functionalised carbene precursors is prepared, each possessing a masked carbene in a 1,5 relationship to a chelating oxo-substituent. Finally, this thesis discusses the attempted *in-situ* preparation of several transition metal complexes and their application a range of organic transformations.

The thesis terminates with a full description of the experimental procedures used and the compounds prepared.

DECLARATION

The research described in this thesis is, to the best of my knowledge, original except where due reference is made to other authors.

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Acknowledgments

I would like to thank both Willie and Robyn for the fantastic opportunity they gave me to work with them over the last three years – not a week went by without me learning something. At the beginning of this thesis Simon Elwood of Quest international and Andreas Danopoulos began as industrial and academic supervisors, and have now become good friends, always willing to help and offer supportive words – I appreciate everything you have done for me.

I am especially grateful to Mary O' Sullivan, the lady who first brought the pleasure of chemistry into my life, and demonstrated the power of enthusiasm to me. Without people such as her, Matt Walker, Darren Caine, Pete Shapland and Richard Ward, this PhD would never have even started – for taking the time teach me the basics, to answer every question, and put me on the right track I want to thank you.

Of course starting a PhD is only the beginning of a life changing experience (!), and it is not possible to complete it without the support of other people. To all members of *the dark side* - in particular Alex, Lorna, and Tom, I couldn't have done it without you, and I hope you keep the special spirit and attitude we developed alive in every lab you go to!

It is very easy to lose track of reality during the years spent researching a PhD thesis and during this time some very close (and tolerant) friends are needed – Mark and Dominic, GuiGui, Camilla and in her very special way, Jojo, have kept everything in perspective for me. Of course, without Saeed (Captain!), the journey to the lab every morning would have been significantly more difficult.

I'm very grateful to Abil Aliev and David Butler for NMR, John Hill and Steve Firth for MS, and Jill Maxwell for microanalysis, for their help in creating and interpreting the data without which, we would all be lost. Also to everyone who has helped me, kept me sane and made the last three years so enjoyable – cheers!

Для оптимиста, неудача - только отсроченный успех.

Abbreviations

Ac	acetyl
Ar	unspecified aryl group
arom	aromatic
Boc	*tert*-butoxycarbonyl
Bu	butyl
Bn	benzyl
br	broad
Bz	benzoyl
c	cyclo
CI	chemical ionisation
Δ	reflux
dba	dibenzylideneacetone
DCC	dicyclohexylcarbodiimide
DCE	dichloroethane
Decomp.	decomposition
DMAC	*N*,*N*-dimethylacetate
DMAP	4-*N*,*N*-dimethylamino pyridine
DME	Dimethoxyethane
DMF	*N*,*N*-dimethyl formamide
DMSO	dimethyl sulfoxide
EI	electron impact
ee	enantiomeric excess
eq	molar equivalent(s)
Et	ethyl
EtOH	ethanol
FAB	fast atom bombardment
FTIR	Fourier Transform Infra Red
g	gram(s)
GC	gas chromatography
h	hour(s)
HPLC	High performance Liquid Chromatography

HRMS	High Resolution Mass Spectrometry
Hz	Hertz
i	*iso*
IR	Infra-Red
IPA	isopropyl alcohol
J	coupling constant
KHMDS	potassium bis(trimethylsilyl)amide
L	unspecified ligand
lit.	literature value
M	unspecified metal
m	medium
m	*meta*
Me	methyl
MeCN	acetonitrile
MeOH	methanol
Mesityl	2,4,6-trimethylphenyl-
min	minutes
mL	millilitre(s)
mp	melting point
MPV	Meerwein-Ponndorf-Verley
MPVO	Meerwein-Ponndorf-Verley-Oppenauer
MS	Mass Spectrometry
n	*neo*
NBD	norbornadiene
NMO	*N*-methylmorpholine oxide
NMR	nuclear magnetic resonance
Nu	nucleophile
o	*ortho*
OTf	Triflate
p	*para*
pip	piperidine
ppm	parts per million
Ph	phenyl
Phth	phthalimide

pr	propyl
py	pyridine
s	strong
R	unspecified carbon substituent
rt	room temperature
t	*tert*
TCCA	Trichloroisocyanuric acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TEA	triethylamine
TMANO	trimethylamine-*N*-oxide
v	volume
w	weak
X	halogen
Y	functionalised group

Chapter 1

Carbenes

1.0 Introduction

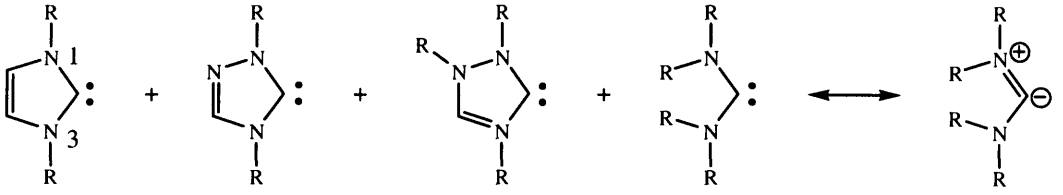
The aim of this thesis is to develop novel ligands for transition metal catalysed reactions, incorporating a diamino-carbene moiety as the point of complexation between the metal and the organic ligand. Diamino-carbenes are now viewed as an alternative to the ubiquitous phosphines, and are occasionally viewed as a substitute for ligands that coordinate *via* nitrogen. Throughout this thesis we will present several classes of novel carbene precursors, which we have developed including pincer, imidazolium, N-amino-imidazolium and 1,2,4-triazole based derivatives. We will discuss the reasons for this choice of scaffolds in detail later in this thesis, but we considered that they might be able to offer a variety of interesting frameworks for alteration of the electronics at the metal centre, and a variety of chelation methods.

In the present introductory chapter, it is therefore appropriate to provide two brief overviews of reference. Thus, we will discuss carbenes and their exploitation to date, after which a second review chapter on hydrogen transfer reactions will be presented. Hydrogen transfer reactions, which result in oxidation or reduction of a substrate are key reactions in organic chemistry and so have been the focus of extensive research. This field is reviewed in order to put our own work within this area into context. Following on from this, we shall present several discreet chapters on a variety of transition metal catalysed reactions in which the activity of these novel diamino-carbene ligands has been investigated.

The opportunity to control the catalytic properties of a homogeneous transition metal based catalyst by tuning both the steric and electronic properties is a very attractive proposal. A degree of control can be exerted on phosphine supported homogeneous transition metal complexes by making small changes to the ligand structure. These changes can in part be directed by the use of the Tolman map of electronic and steric effects.[1] *N*-heterocyclic carbenes (NHC's), derived from the substitution of the C-2 proton on an imidazolium salt by a metal, have been known for many years,[2] but interest lay dormant until the research efforts of Arduengo *et al.* resulted in the isolation of the free bis-adamantyl imidazol-2-ylidene carbene in 1991.[3] The application of these compounds as ligands for catalysis has only started to become a major focus of study

within the last 10 years, and has been led by the research group of Herrmann.[4] Spectroscopic studies have shown that NHC complexes form strong bonds to late transition metals since they are excellent σ-donors and generally possess minimal π-back donation capabilities, similar to their organophosphine counterparts.[5]

Further work has shown that the two ligand classes possess distinct electronic properties,[6] with NHC's being more strongly electron donating than even the most basic phosphines.[7] The fan shaped steric profile of NHC's is also different from the cone shape of a PR_3 ligand,[1] but this has yet to be fully exploited. Studies have shown that nucleophilic N-heterocyclic carbenes represent a very versatile class of ligands due to their interesting steric and electronic properties.[8] It is simple to incorporate very bulky groups such as mesityl (1,3,5 tri-methylphenyl-), super-mesityl (1,3,5 tri-*tert*-butylphenyl-) and adamantyl on the nitrogen atoms at positions 1 and 3 and to vary the steric size of these groups in order to develop a specific steric environment.[9] The bonding in a NHC complex is best treated as a diaza-allyl system, with a degree of π–aromaticity being present in the unsaturated C-C (**1**) and C-N (**2**, **3**) species illustrated in Figure 1.



1 **2** **3**

Figure 1

NHC's have rapidly been accepted as a new class of ligand, capable of mimicking the well-established phosphines, but without the classical problems associated with the use of the latter, which will be detailed and discussed later. The recent use of NHC moieties is not only restricted to catalysis using late transition metals, they have also been used in their own right as organic catalysts or as reactants in multi-component reactions.[10] Their use as ligands has several advantages over the commonly utilized phosphines. They exhibit a greater stabilising effect, higher thermal stability, and a greater resistance to dissociation from the metal centre.[11] Unlike phosphines, because of their enhanced donor properties, an excess of the carbene ligand is not required in order to prevent

ligand loss from the catalyst, which results in bulk metal deposition. Consequently, an increasing number of catalytic reactions make use of nucleophilic carbenes as catalyst modifiers.

1.1 Carbenes

Since the electronic nature and stability of the carbene ligands is the central feature of this thesis, the following sections are devoted to the nature and understanding of these reactive species. A carbene is a neutral, divalent carbon atom, containing six valence electrons, only four of which are involved in bonding. The remaining two electrons reside on the carbene carbon atom and can adopt one of two possible configurations. The two electrons can have anti-parallel spin and exist one, in an sp^2 orbital and the second in a p-orbital. This arrangement of electrons is termed a triplet carbene. A second arrangement has both electrons spin paired in a single sp^2 orbital and this latter arrangement is called a singlet carbene. The carbene carbon in both cases is formally in a +2 oxidation state, and has no charge (Figure 2).

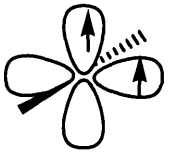
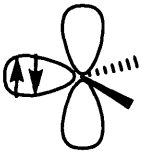
Triplet Carbene	**Singlet Carbene**
	
Substituents adopt near linear geometry	Substituents adopt a bent geometry
1 electron in an sp^2-orbital 1 electron in a p-orbital	2 electrons in an sp^2-orbital
sp-type hybridisation	sp^2-type hybridisation
Di-radical character	Ambiphilic character

Figure 2

Triplet carbenes behave as diradicals as they have two singly occupied orbitals, in contrast to singlet carbenes, which have one occupied orbital, and a second higher energy, empty orbital. This degenerate orbital arrangement is what gives singlet carbenes their ambiphilic character. In the simplest valence bond representation, this is often shown as a carbon atom possessing both a positive and a negative charge as represented in Figure 3.

Figure 3

The relative energies of the σ-type and π-type orbitals of the carbene are greatly influenced by the substituents attached to it, and alteration of the relative energies of these two orbitals dictates the configuration of the electrons, into either a singlet or triplet state. This explains the observed dependency of ground state multiplicity on the substituents. Substituents displaying σ-electron withdrawing capability stabilise the singlet state by increasing the *s*-character of the occupied orbital. A more significant stabilisation effect is realised when the adjacent substituents are good π-donors. The resulting increased energy of the vacant *p*-orbital, caused by the delocalisation of electron density from the substituent lone pairs (Figure 4), stabilises the singlet state as it becomes more difficult to promote an electron into this high energy orbital, as is required were the molecule to attain the more reactive triplet state.

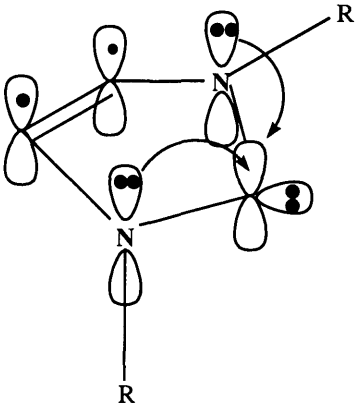


Figure 4

Donation of both substituents' lone pairs results in a four electron, three-centre π system, which results in partial multiple bond character between the carbene and the attached heteroatom(s), giving a degree of negative charge on the carbene carbon. This bonding arrangement also minimises further electron donation onto the carbene carbon atom *via* backdonation from the metal when a complex is formed as summarised in Figure 5.

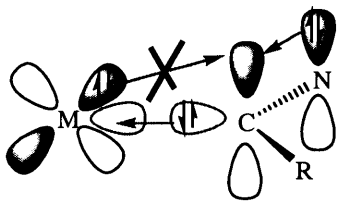


Figure 5

The ambiphilic nature of singlet free carbenes is apparent both from nucleophilic type reactions occurring through the occupied sp^2 orbital, and also by nucleophilic attack on the vacant *p*-orbital. Nucleophilic attack on the *p*-orbital is minimised in the diamino class of free carbenes for the reasons outlined previously, i.e. the electrophilicity of the 'vacant' *p*-orbital is severely compromised due to the mesomeric effects of the substituents.

Carbene metal complexes can be divided into two broad subdivisions, those of the Fischer[12] and Schrock types (Figure 6).[13]

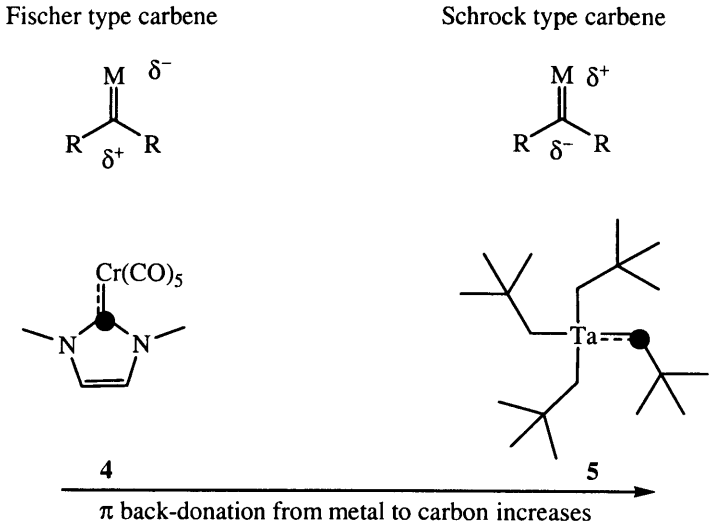


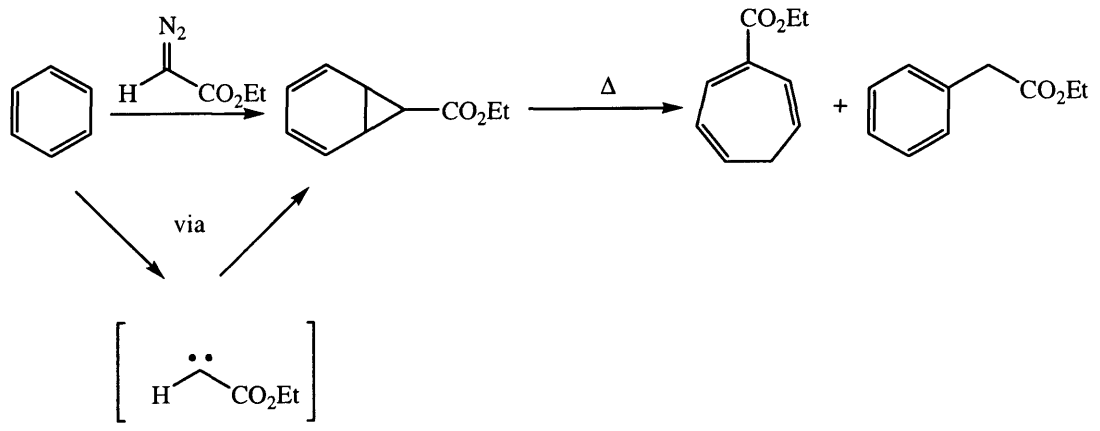
Figure 6

Fischer type carbene complexes, e.g. **4**, are defined as being electrophilic at the carbene carbon, and at least one of the R groups (Figure 6) must be a heteroatom, while Schrock type complexes are nucleophilic at the carbene carbon and the R groups are either alkyl or H. Schrock type complexes, e.g. **5**, experience a strong π-interaction between the metal and the carbene, and because of this, the carbene develops an energy rich π^* orbital minimising its susceptibility to nucleophilic attack. Due to the good orbital

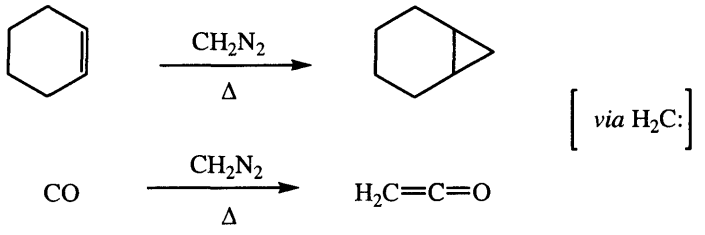
overlap between the occupied *d*-orbital of the metal and the vacant carbene *p*-orbital, electron density can be easily transferred to the relatively electron deficient carbene from the metal, further reducing the likelihood of nucleophilic attack by increasing its nucleophilic character. There is minimal π-backbonding from the metal to the carbene with Fischer type carbenes, because of the effect of the adjacent heteroatoms, resulting in a lower energy π^* orbital. The poor molecular orbital overlap between the metal and the carbene also prevents movement of electronic charge from the metal to the carbene, with the consequence that this type of carbene is vulnerable to nucleophilic attack.[14]

Although the foregoing theoretical analysis provides a very useful predicture rationale for the relative stability and reactivity of carbenes and their metal complexes, it is also of interest to examine synthetic endeavours in this area. Attempts to prepare the parent carbene (H_2C:) by dehydration of methanol were reported as early as the 1830s.[15] At that time, the tetra-valency of carbon had not been established, and therefore the existence of stable carbenes was considered quite reasonable. Nearly 50 years later, following the discovery that carbenes posses only six valence electrons, and thereby defy the octet rule, led researchers of the time to believe that it was impossible for such species to exist.[16] Thus, the quest for stable carbenes was viewed as unreasonable and remained so for some time. Although interest in synthesising and isolating carbenes had waned, reactions in which they were postulated as key intermediates were published.[17] Notable examples are the Büchner ring expansion reaction,[16a] Staudingers' cyclopropanation reaction[16b] and the dihalocarbene reactions of Doering (Scheme 1).[16c]

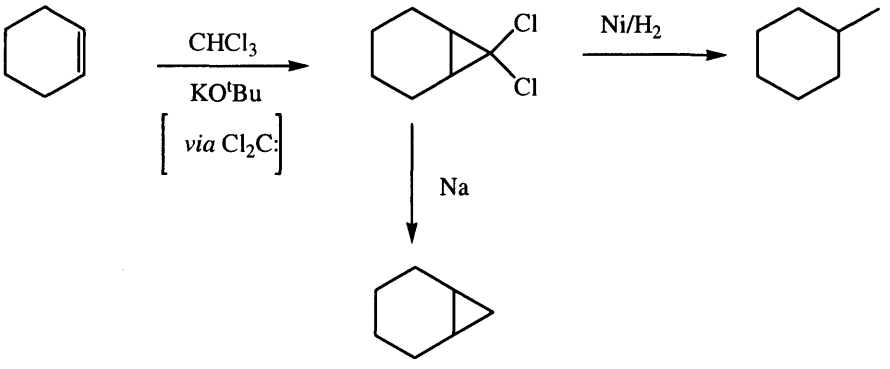
Buchner Ring expansion



Staundinger

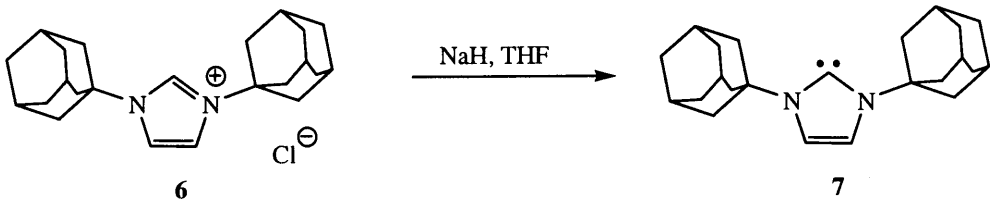


Doering dihalocarbene



Scheme 1

Almost 40 years have passed since the first complexes containing *N*-Heterocyclic carbenes (NHC's) were independently published by Wanzlick[18] and Öfele[19] in 1968, yet it was not until publication by Arduengo, in 1991, of a stable, free, isolable NHC **7** (Scheme 2) that the current intense research activity within both academic and industrial communities of these species began.[20]



6 7

Scheme 2

The interest in *N*-Heterocyclic carbenes and their complexes lies in their unique properties. They are very strong σ-donating ligands and due to the adjacent heteroatoms, are poor acceptors of backdonated π-electrons from the complexed metal. This makes NHC's more comparable to traditional phosphorous or nitrogen based ligands, than to classical carbenes.[21,22] The carbene-metal bond has been shown to be chemically and thermally inert, and also demonstrates a very high dissociation energy from the metal.[23] These properties in particular make NHC based ligands suitable for use in catalysis, where reaction conditions can often lead to decomposition of traditional transition metal catalysts. NHC complexes have proved their suitability in a wide range of important transformations, which will be discussed in further detail later. The potential for functionalising NHC's provides enormous scope for ligand design, with simple modification of steric and electronic factors possible. There have been a variety of reviews published on NHC ligands and their applications,[24] as well as their comparison to phosphines.[25]

1.2 Towards stable carbenes

1.2.1 Triplet Carbenes

In the last 20 years, the preparation of persistent triplet carbenes such as **8** (Figure 7) and the isolation at room temperature of singlet carbenes such as those in Figure 9 represent great progress. Triplet carbenes are generally felt to be too reactive to be isolated as there is no thermodynamic stabilisation possible. However, Zimmerman,[26] and more recently Tomoika[27, 28] have had success in isolating such carbenes. The most persistent (*vs.* stable) triplet carbene to have been isolated is the bulky, biaryl **9** (Figure 7),[29] where the large amount of steric bulk and extensive conjugation allow for good delocalisation of the non-bonding electrons which act to minimise dimerisation. Blocking of potential 'leakage' sites of the delocalised electrons, which could also result in dimerisation, using alkyl groups, is another common method employed to stabilise these species. The triplet carbene **8**, exists in solution with a $t_{1/2}$ of 16 seconds, but is indefinitely stable at room temperature in the crystalline form.[29] The more recent example **9** is stable for 1 week in solution at room temperature.[27f] The instability of these triplet carbenes can be further understood when considering that the resonance structures achieved by delocalisation of the electrons of the triplet carbene involves disruption of the aromaticity of the substituents and hence this stabilisation is only achieved at a high energetic cost.[30]

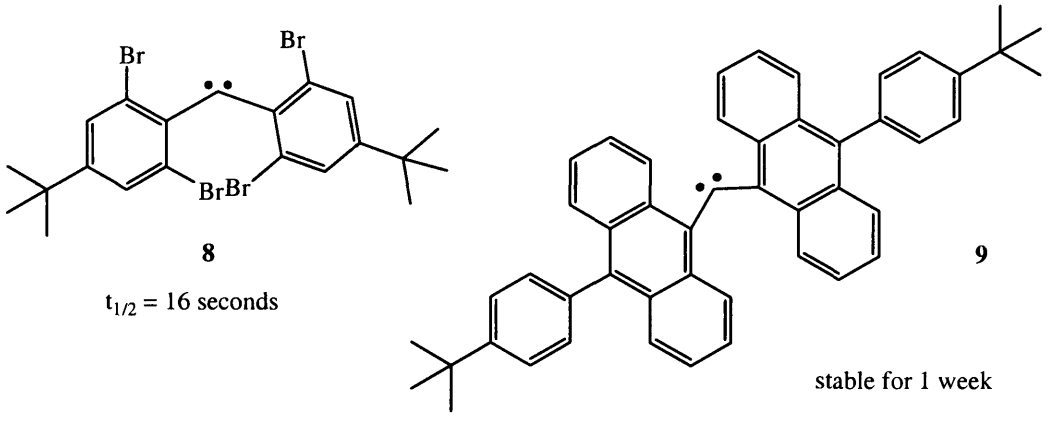
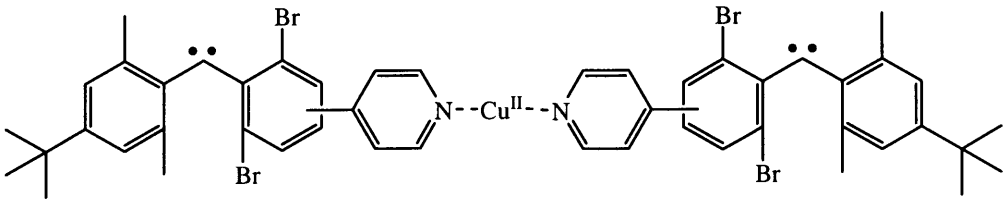


Figure 7

One of the most recent achievements is the complexation of a triplet carbene with copper (**10**),[31] which demonstrates a method that shows the potential to allow simpler access to high spin carbene systems (Figure 8).



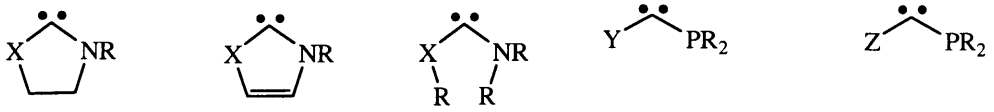
10

Figure 8

At the time of writing no crystal structure of a triplet carbene has yet been published and one of the most sought after achievements in the field is to be able to prepare a carbene which could be isolated in both the singlet and triplet state.

1.2.2 Singlet Carbenes

Singlet carbenes, unlike their triplet counterparts, have simple methods available for their stabilisation and account for the vast bulk of the literature on isolable carbenes. The ability to tune the reactivity of these species *via* steric or electronic modification makes them very attractive species for application as ligands. A wide variety of singlet carbenes have been synthesised, both cyclic and acyclic, using a variety of heteroatoms and combinations of heteroatoms coupled with varying degrees of saturation,[24] some of the more common species encountered in the literature[32] being illustrated in Figure 9.

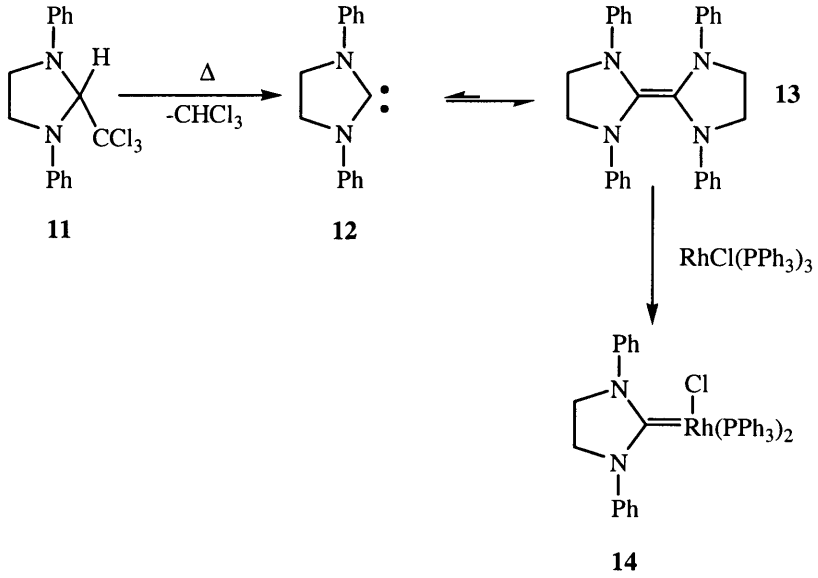


X	NR, S, O
Y	R, SiR_3, PR_2, 2,6-$(CF_3)_2C_6H_3$
Z	CF_3, SF_3

Figure 9

One of the most common reactions of singlet carbenes is dimerisation,[33] and increasing the steric bulk around the carbene has become a common strategy for preventing this problem, which often hampers attempts to isolate the free species. An equilibrium

between the carbene in its free form **12**, and the electron rich olefin dimer **13** has been shown to exist in a range of systems.[34] An interesting observation by Lappert is that these electron rich olefins can undergo a metathetical cleavage with complexes such as tris(triphenylphosphine) rhodium (I) chloride (Wilkinson's catalyst) or rhodium COD chloride dimer, to form the metal carbene complex **14** (Scheme 3).[35]

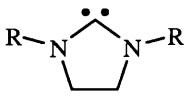


Scheme 3

A further method used to minimise dimerisation, is to increase the extent of π-conjugation in the system. To this end, carbene scaffolds such as imidazole-2-ylidene **16** and benzimidazole-2-ylidene **17** (Figure 10) have proved successful in allowing less sterically hindered free carbenes to be isolated.[36]

1.3 *N*-Heterocyclic singlet carbenes

Most of the carbenes in the literature, which are singlet carbenes, are also *N*-heterocyclic.[32b] There are several common varieties of heterocycle used to support the carbene functionality, but the most utilised is imidazole-2-ylidene **16**.

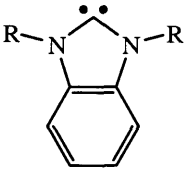


imidazolin-2-ylidines

15

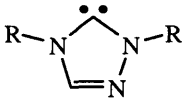
imidazol-2-ylidenes

16



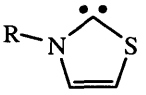
benzimidazol-2-ylidenes

17



1,2,4-triazol-5-ylidenes

18

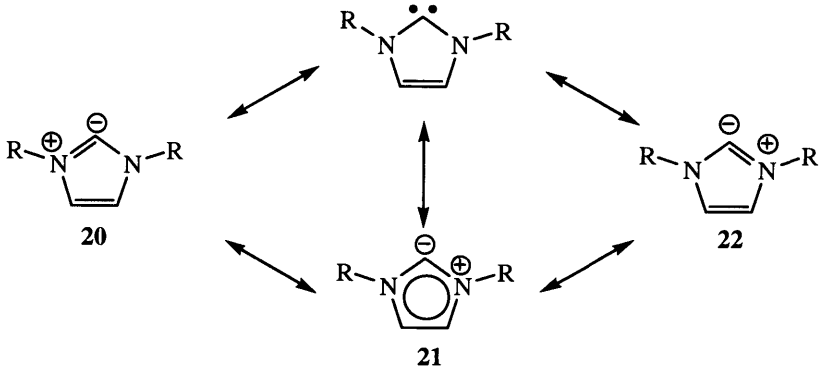


1,3-thiazol-2-ylidenes

19

Figure 10

This is due to their simple preparation and enhanced stability over the alternative structures. Imidazole-2-ylidenes are aromatic, albeit less so than their imidazolium cation precursors, or for example simple aromatic systems such as benzene.[37]



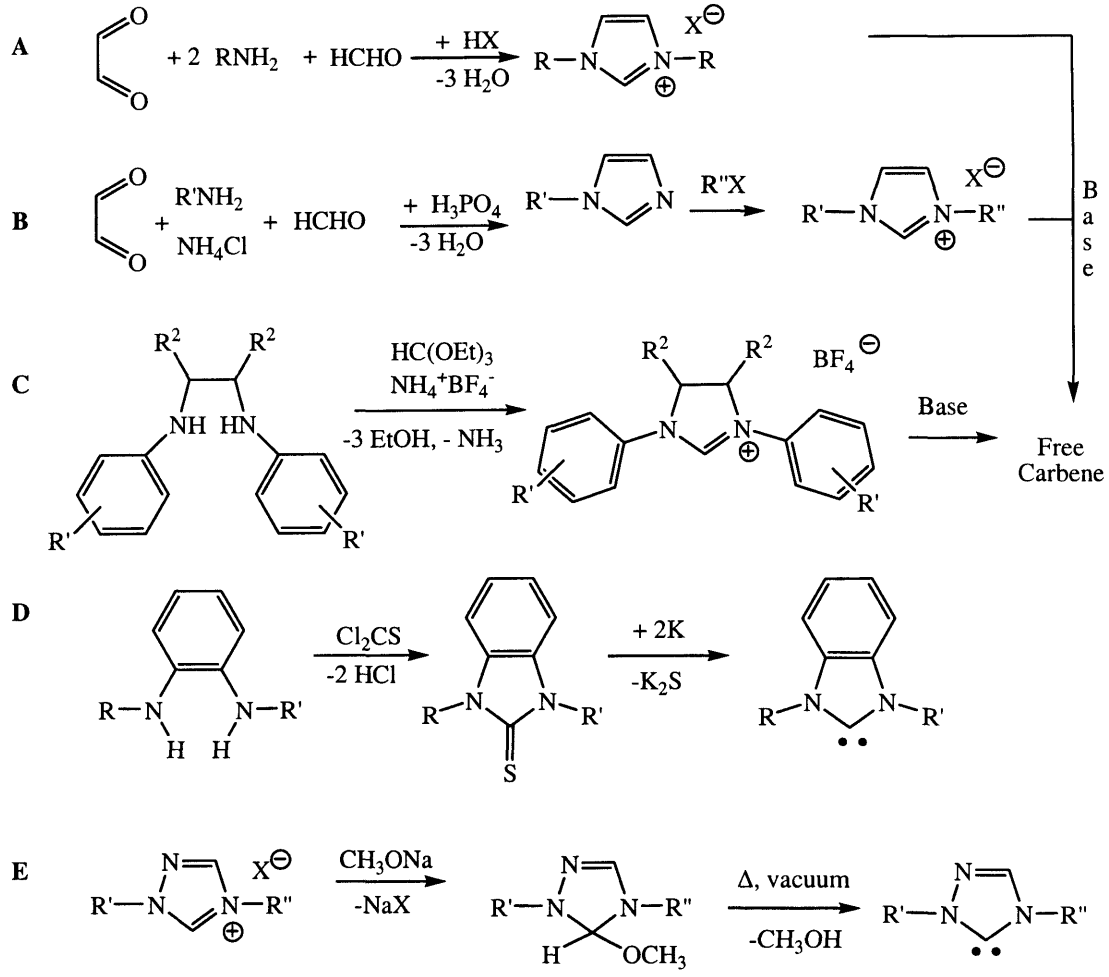
20 **21** **22**

Scheme 4

As detailed in Scheme 4, imidazole-2-ylidenes can be represented as a combination of several resonance forms, giving partial double bond character to the carbene-nitrogen

bonds. These proposed tautomeric structures **20** - **22** are verified by the bond lengths observed in X-ray crystal structures lying between that of a typical single (1.47Å) and a double C-N bond (1.29Å).[38] The aromaticity of the unsaturated ring system provides additional stability to the carbene, rendering it less reactive, and hence less likely to dimerise than its saturated imidazolin-2-ylidine analogue. When Wanzlick proved the existence of a singlet carbene in 1962,[39] he was unable to isolate the free species and it is likely to be the non-aromatic nature of his carbene that thwarted his attempts, in contrast to the work of Arduengo who synthesised an aromatic carbene **7**, and gained repute for the first isolation.[40]

There are many methods available for the synthesis of NHC species, some of which are outlined in Scheme 5. Methods A - C all require the formation of an imidazolium salt, which is then treated with a strong non-nucleophilic base to generate the free N-heterocyclic carbene. Methods D and E differ insomuch as they both require a formal α-elimination sequence.



Scheme 5

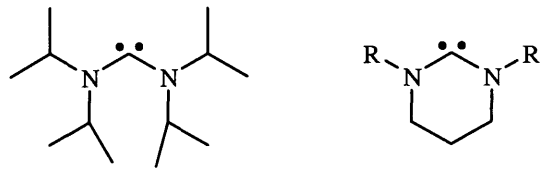
In view of the large variety of methods for the synthesis of imidazoles,[24] there is great scope for incorporating alternative side chains with the carbene nucleus and this has been demonstrated with such functionalisation as imine,[41] ferrocenyl[42] and bis(cyclopentadienyl)dichloroytterbate[43] substituents, long fluoroalkylated[44] and alkyl[45] chains as well ribofuranose groups[46] and polymer supported[47] carbenes. Other syntheses have resulted in NHC's with chiral substituents or chiral backbones,[48] secondary donor groups such as phosphines,[49] and oxazolines[50] as well as links to other carbenes, providing bi,[51] tri[52] and even hexa-dentate[53] carbenes.

1.4 *N*-Heterocyclic carbenes as ligands

Since the initial publication of an NHC-metal complex by Wanzlick,[18] the focus of many researchers has been the application of NHC's as ligands, rather than studying them as separate entities. The isolation, purification and characterisation of the free carbene is not always simple, yet the corresponding metal complexes generally offer much greater stability, including increased tolerance to ambient conditions. A particular strength of NHC based molecules as ligands is their capability to coordinate to metal centres, ranging from electron rich transition metals e.g. Pd (0), Rh (I) and Ru (II), electron poor main group metal cations, such as Be^{2+} and high oxidation state metals such as Ti (IV), Nb (V) and Re (VII).[24b] NHC's offer exciting new possibilities as a new class of nitrogen containing ligands. Simple nitrogen donor compounds were used only rarely in the 1970s and 1980s as ligands and eventually fell into disrepute because of the observation that amines 'poisoned' palladium catalysts in catalytic hydrogenation. Some of the first asymmetric catalysts were heterogeneous nitrogen containing chiral systems, such as silk fibron with palladium,[54] and amino acid modified Raney nickel, both of which were used for reduction. The use of platinum modified with cinchona alkaloids has also received a lot of attention for reducing α-ketoesters,[55] and a review published by Togni and Venanzi summarised many of the promising results that have been noted for nitrogen containing ligands in the field of catalysis.[56]

In parallel with the coordination chemistry of ethers, amines, isonitriles and phosphanes, NHC's act as two electron, σ-donor ligands,[57] and are even stronger σ-electron donors than amines. The σ-donor properties have been compared favourably to that of the electron rich phosphines,[58] and it has been shown that back donation from the metal centre is insignificant,[58a,b] as one would expect because of the high-energy vacant p_π orbital of the carbene. It is this lack of electron accepting capability that led NHC's to become referred to as 'nucleophilic' carbenes. The metal carbon bond of a NHC complex is much less reactive, than either a traditional Schrock or Fischer type carbenes, exhibiting minimal double bond character,[59] whilst remaining a very strong bond, resulting in these complexes being ideal for use as ligands in catalytic reactions. The pronounced σ-donation capacity of NHC's in combination with their poor π-acceptor properties is considered to be one of the major advantages of this class of

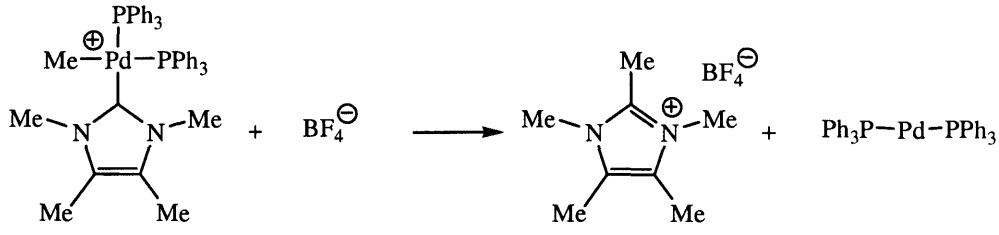
ligand. Therefore it is of particular interest to note that the acyclic diaminocarbene **20** is an even stronger σ -donor than its cyclic counterparts,[60] and the six-membered ring diaminocarbene **21** appears to be thermodynamically stable to dimerisation, unlike its five-membered analogue[61] yet neither of these species have, as yet, been explored as ligands (Figure 11).



20 **21**

Figure 11

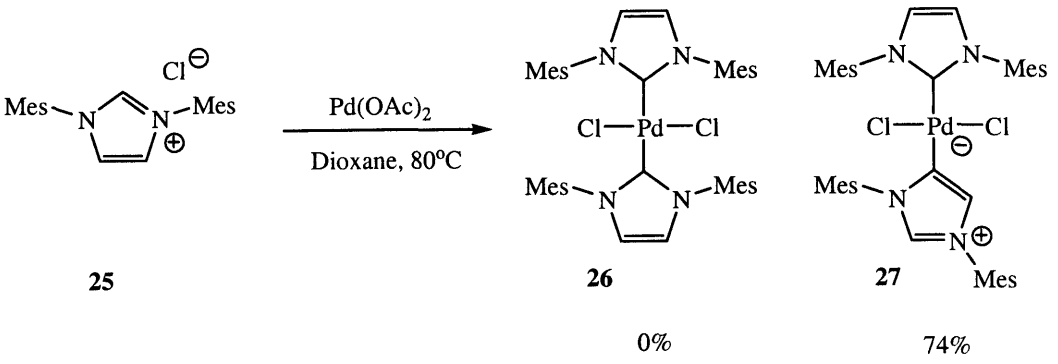
Although an NHC ligand usually coordinates strongly to the metal, it has been shown that decomposition of the metal carbene bond is, in theory, possible. Cavell has demonstrated using computational methods that the NHC-metal bond of **22** can be ruptured (Scheme 6). However, as this work is currently only theoretical,[62] a degree of confidence in the remarkable chemical inertness of the carbon-metal bond can still be held true.



22 **23** **24**

Scheme 6

Imidazol-2-ylidenes most often bind to the metal *via* C_2, as this is the location of the most acidic proton, prior to formation of the carbene, but *in-situ* methods for producing carbenes can result in unusual binding motifs.[63] This unusual binding generally occurs through $C_{4/5}$ of the imidazolium ring, as can be seen in Scheme 7, and is an example of pseudo η^3 binding rather than the usual direct carbene coordination. This observation is highly unexpected, as this area of the ring is considered inert.[64]



Scheme 7

None of the desired compound **26** was recovered from the reaction in Scheme 7, only the cationic species **27** and its production is very dependant on the base and the metal source used.[65] This sort of binding is poorly understood, but appears to happen only for *in-situ* methods, and has not been observed when combining a free carbene and a metal source. This has the implication that any complexes made *via* in-situ methods must be isolated and characterised before being used, as the structure cannot be predicted with complete confidence.

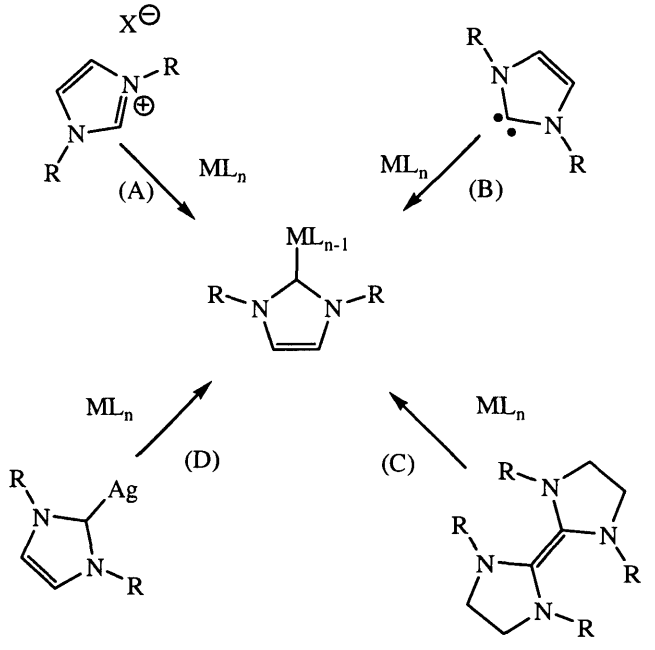
From his many structural and thermochemical studies Nolan stated that "in general, these ligands behave as better donors than the best phosphane donor ligands, with the exception of the sterically demanding (*bis*-adamantly N-heterocyclic) carbene."[66] Comparisons between phosphine and NHC ligands are common but the two classes are distinct in electronic properties,[6] and steric profile.

Replacement of the well established phosphine ligand with a NHC analogue has several key advantages. The role of a phosphine ligand is to support the metal centre in the form of a stable ML_x species, which is capable of entering a catalytic cycle. However, reaction conditions such as those used during many metal catalysed coupling reactions, such as the Heck reaction[67] lead to ligand dissociation and early deposition of elemental metal resulting in deactivation of the catalyst as an unwanted side reaction.[68] To prevent metal deposition, excess phosphine (2-4 eq) is used but this has several negative implications. Not least, the electron rich phosphines, such as those typically used as ligands, are expensive and difficult to remove from the final product. At times phosphine ligand based catalysis uses relatively high loading in the region of 5 mol% and this can add significant costs during the manufacture of bulk compounds.[69] Excess

ligand also reduces the reaction rate and must be counterbalanced by adding larger quantities of transition metal to achieve adequate activities.[70] Phosphine-metal complex decomposition (especially ruthenium based complexes) yield highly coloured, difficult to remove by-products which poses a problem, especially in the fine chemical and pharma industries.[71] When the triphenylphosphine ligand is not appropriate, substitution with trialkyl ligands is possible, however these can produce complexes that are unstable towards air, moisture and heat,[72] making them difficult to handle. A further problem associated with phosphines is their low stability towards oxidation, making it is almost impossible to recycle either the ligand or the catalyst. In consequence it is hoped that NHC ligands, with their orthogonal characteristics, may overcome some of the traditional problems of phosphines, whilst maintaining their advantageous characteristics.

1.5 *N*-Heterocyclic carbene complexes

Following the simultaneous reports by Öfele[19] and Wanzlick[20] of the first NHC complexes, there was an initial paucity of publications demonstrating new NHC metal complexes, due to the difficulty in producing such species. With the discovery of stable free *N*-heterocyclic carbenes in 1991 however simplified and more direct routes to these complexes became available,[73] and with this, a resurgence of interest.



Scheme 8

Many techniques to access NHC complexes have been developed and published, some of which are summarised in Scheme 8. The four general methods outlined above represent the most common synthetic methods for accessing metal complexes of NHC ligands.

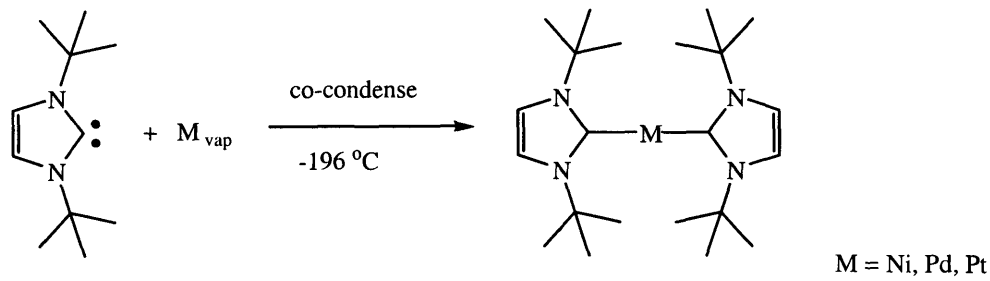
(A) Deprotonation of the imidazolium salt *in situ* using, for example, basic anions, basic metallates (i.e. Ag_2O) or an external metal base, in the presence of a suitable metal precursor.[74]

(B) Combination of an isolated free NHC with a suitable metal precursor.[75]

(C) Cleavage of electron rich olefins, Wanzlick dimer type molecules, under thermal conditions in the presence of a suitable metal precursor.[58c]

(D) Transmetallation of the carbene ligand (e.g. silver carbene to palladium carbene).[76]

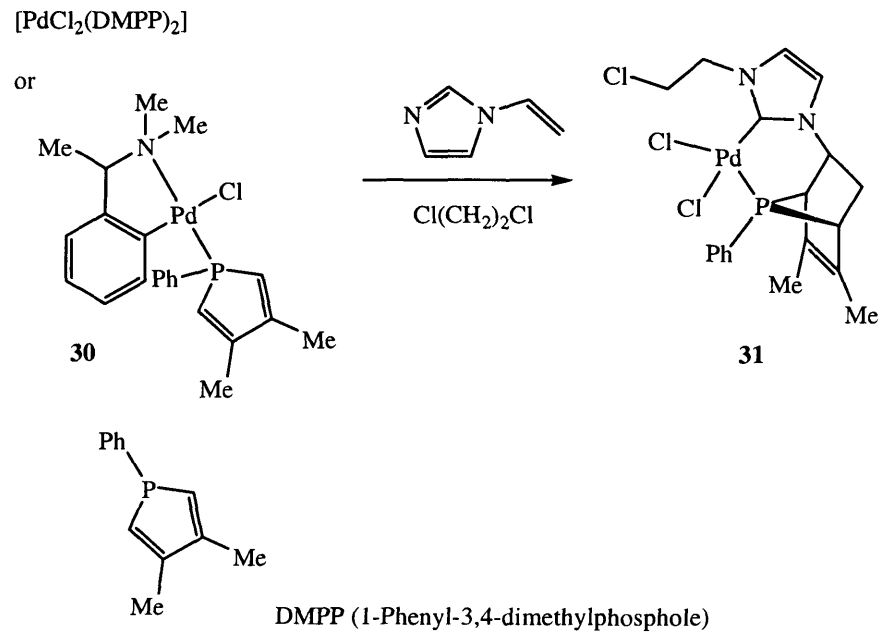
In addition to these general methods, other more specific techniques have been developed for the formation of a metal complex, such as vapour phase synthesis (Scheme 9)[77]



28 **29**

Scheme 9

and metal template synthesis (Scheme 10).[78]



30 **31**

Scheme 10

The deprotonation method (A, Scheme 8) typically uses relatively strong bases such as *n*-BuLi, which presents potential complications in that alternative sites may be

deprotonated. To overcome this problem, alternative bases than n-BuLi, such as K(N(TMS)$_2$), KH or KO*t*Bu were introduced in conjunction with liquid ammonia or THF as preferred bases and solvents for generating the free carbene. Direct metallation of the imidazolium salt with basic salts such as Pd(OAc)$_2$ has also proved successful, although the temperature initially required was high (refluxing DMAC, 166°C), but subsequent methods use much milder conditions (Cs_2CO_3, 80°C).[79]

N-Heterocyclic carbene complexes have been made with the vast majority of elements in the periodic table as shown by the highlighted elements in Figure 12. Every transition metal apart from those of the bottom row has been incorporated into a complex. Thallium,[80] copper silver and gold,[58b] nickel and palladium,[73] rhodium and iridium,[57f] iron,[51a] ruthenium,[23a] osmium,[51b] technium,[81] rhenium,[82] chromium,[24b] molybdenum and tungsten,[83] vanadium, niobium, tantalum, titanium, zirconium and hafnium,[57a] and scandium,[84] provide a few examples.

H																He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac	Rf	Db	Sg	Bh	Hs	Mt	Unn								

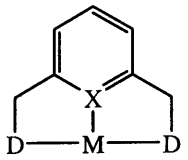
Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Figure 12

1.5.1 Pincer complexes

A recent development in NHC complex formation is the emergence of the pincer ligand.[85] Organometallic complexes containing tridentate, monoanionic ligands were reported in the late 1970's,[86] and these type of complex became known as 'pincer ligands'.[87] The essential characteristics that a complex requires to be termed 'pincer' are that it posses a central metal atom held in place by a tridentate ligand. The ligand is connected to the metal atom *via* at least one carbon-metal σ-bond. Further substituents

can then coordinate to the metal site *via*, for example, O, S, N or P donor atoms (Figure 13).



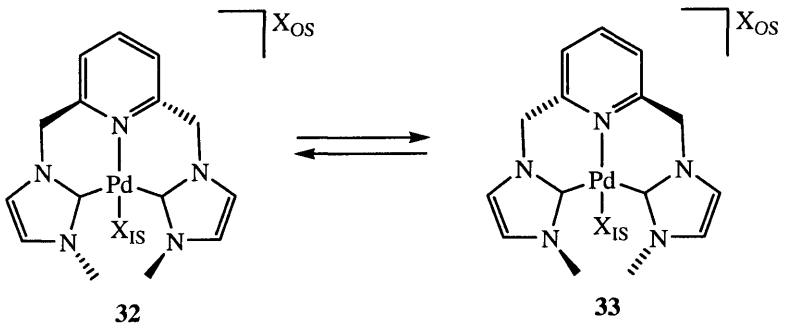
D = Donor atom
M = Metal atom
X = N, C

Figure 13

Pincer complexes where D, in Figure 13 is phosphorous first appeared in the 1970's.[86a] In this case the trivial assignment PCP-pincer complex can be used, which refers to the actual arrangement of the chelating atoms around the metal centre, i.e. ***P***hosphorous-***C***arbon-***P***hosphorous. Other common complexes are NCN, SCS and CNC. In the case of the CNC pincer, there are two metal-carbon σ-bonds. As it is the metal-carbon bond of the N-heterocyclic carbene unit that is the key to the high stability of a pincer complex, it is advantageous to have multiple bonds of this type.

The most frequently observed bonding system seen with pincer complexes, to their metal centre, is the meridonal η^3-like coordination mode. This arrangement results in the ligand binding to the metal centre as a six-electron donor in the case where X = nitrogen in Figure 13, with the neutral donors positioned *trans* to each other on the metal. This bonding mode requires the central pyridyl ring of the pincer ligand to assume a conformation which is approximately coplanar with the coordination plane of d^8 square-planar metal centres such as Rh (I), Ir (I), Ni (II), Pd (II) and Pt (II). In the case of d^6 square-pyramidal metal geometries, including Ru (II), Rh (III), and Ir (III), the pyridyl ring of the ligand becomes coplanar with the basal plane of the metal.[88] It was unexpected therefore, when displacement of the central pyridine ring of a CNC pincer was observed to be facile, even occurring during conformational fluxionality of the CNC ring. This observation occurred with the chiral pincer complex **32** when an outer sphere halide coordinated to the metal and converted the pincer to an intermediate chelating bis-carbene ligand, before disassociating from the metal and returning the complex to a pincer type structure once again, with the overall result of inverting the

chirality of the ligand to give **33**, Scheme 11. This entire process was observed to occur on the NMR timescale.[89]



32 **33**

X_{OS} = Outer sphere halide
X_{IS} = Inner sphere halide

Scheme 11

Pincer based molecules provide enormous potential for the modification of various parameters, which can be achieved without significantly affecting the bonding mode and yet still exert an effect on the steric and electronic properties of the complex. The steric environment of the system may be affected by altering the size of the donor substituents or by adding functional groups to the central pyridyl ring. The electronics of the system can be easily tuned by careful selection of the donor group substituents, be they electron withdrawing or donating. Further alteration of the electronic properties of the metal centre can be realised by substitution on the pyridyl ring.

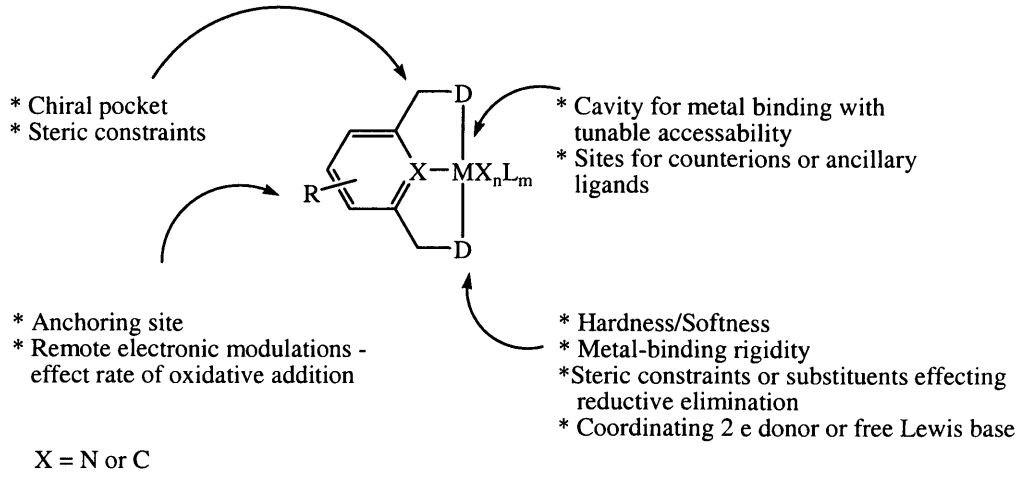


Figure 14

1.6 *N*-Heterocyclic carbene complexes in catalysis

N-Heterocyclic carbene complexes have been shown to have catalytic activity in a wide range of important reactions. Asymmetric allylic substitution using a range of acetates and dimethylmethyl malonate,[90] transesterification/acylation,[91] Suzuki couplings[92] even of hindered aryl systems,[93] Heck,[94] Kumada,[95] and Sonogashira[96] coupling reactions as well as many other palladium catalysed reactions have all been demonstrated.[97] Buchwald Hartwig aminations and C-N coupling reactions,[98] CO-ethylene copolymerisation,[99] olefin metathesis,[100] C-H and C-C activation,[24g] hydrogenation and transfer hydrogenation,[85c] amination,[98c] as well as hydroformylation[101] and hydrosilyation[102] have all also been achieved by NHC supported transition metals. NHC complexes have been immobilised on different solid supports such as polymeric resins[103] and clay,[85c] and although showing good activity, they are usually not as active as the parent complex.[104] Chiral induction has been achieved with NHC catalysis resulting in excellent enantiomeric excess for many reactions.[105] NHC's have been applied to asymmetric catalysis without the use of metals as organocatalytic species.[106] Several excellent reviews have been compiled on the use of NHC complexes for catalysis.[107] Claims that the metal complexes of NHC's are very stable have been substantiated by the fact that the method of preparation of many complexes (polar solvents such as DMSO/DME and high temperature), analysis (reverse phase HPLC with water/methanol solvent), and purification (silica chromatography with no special attention to exclude air), all show that these are remarkably stable complexes. Such conditions would have resulted in decomposition of phosphine based compounds.[108] From this ever-expanding base of experimental data for the use of NHC complexes in catalysis, examples of their numerous strengths over phosphine-supported catalysis are becoming more frequent, especially in reactions where thermal stability is of importance.[109] Some important reactions in which NHC complexes have out performed their phosphine counterparts are presented below.

Olefin metathesis is an area of intensive research activity,[110] spurred on by the easily obtainable Grubbs generation 1 catalyst **34**,[111] as well as molybdenum based Schrock systems.

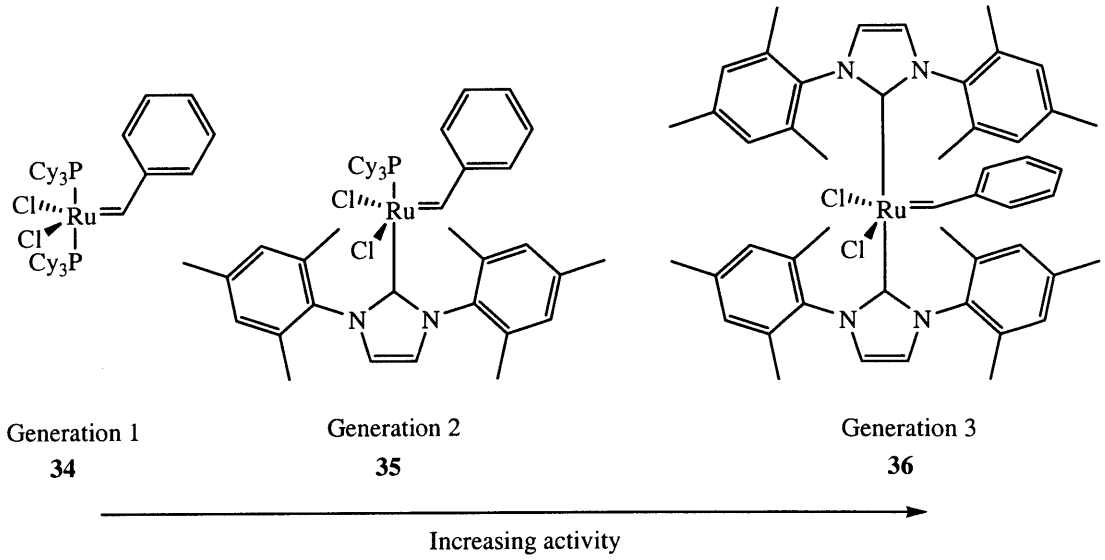
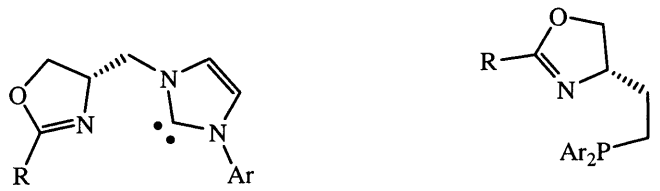


Figure 15

Research in this field has shown the beneficial effect of NHC ligands, for the ruthenium mediated reaction,[112] with improvements to both the robustness and the activity of the initial Grubbs catalyst on replacement of a phosphine with a NHC ligand being demonstrated.[113] It is believed the role of the bismesitylimidazole carbene ligand in particular, is twofold. It is a better donor than PCy_3 as evidenced by enhanced catalytic performance,[114] and its more sterically demanding presence helps to prevent (or retard) bimolecular carbene decomposition.[6b] New more active NHC based, phosphine free catalysts for this transformation are regularly published.[115]

Traditional hydrosilylation catalysis suffers from a number of drawbacks, including the formation of significant amounts (20 to 40%) of undesirable isomeric olefins, reduction of the starting alkene, as well as other side reactions. If these impurities are not removed during workup, they lead to deleterious effects on the properties of the final alkyl-silane materials. In addition, the formation of colloidal Pt species during the course of a hydrosilylation often results in further undesired reactions and colouration of the final product. Use of NHC-platinum based catalysts result in the removal of virtually all of these problems with the required product being recovered almost exclusively.[102]

The asymmetric hydrogenations of *E*-aryl alkenes has been used to compare the two ligands **37** and **38** in Figure 16.

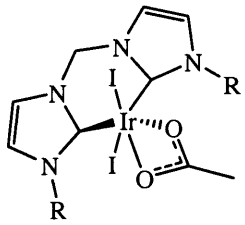


37 38

Figure 16

The results using the carbene ligand **37** gave much improved enantioselectivities over the analogous phosphine **38**. The reasons behind the improved selectivities are not fully understood, however it is known that NHC ligands cannot present edge-face arrays of aryl groups in the same manner as many phosphines do and hence the origin of the enantioselectivity must arise from a different topological feature.[50]

In a similar vein, air-stable and moisture-insensitive Ir catalysts for efficient transfer hydrogenation of ketones containing a chelating bis *N*-heterocyclic carbene ligand **39** have been developed.



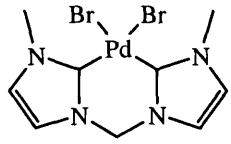
39

Figure 17

Most hydrogen transfer catalysts for this reaction show relative reactivity Rh > Ir, but the reverse relationship was found using an NHC ligated catalyst (Ir > Rh). Tuning of the ligand wingtip substituents, R, greatly increases either the catalyst activity or selectivity. When R = neopentyl, the complex is capable of catalysing the transfer hydrogenation of benzophenone to >98% conversion in only 4 min with a turnover frequency at 50% conversion of 50,000 h^{-1}, but when R = isopropyl, the complex is incapable of reducing bulky ketones.[116]

The catalytic conversion of methane into methanol is a major challenge. Methane, as the major constituent of natural gas, is currently the cheapest source of hydrocarbons. Hermann *et al* have demonstrated the unprecedented activity of a palladium NHC

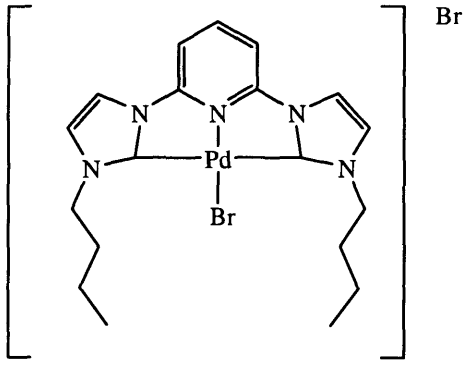
complex **40** under the acidic conditions that are a necessary mechanistic prerequisite for C-H activation of methane to methanol.



40

Figure 18

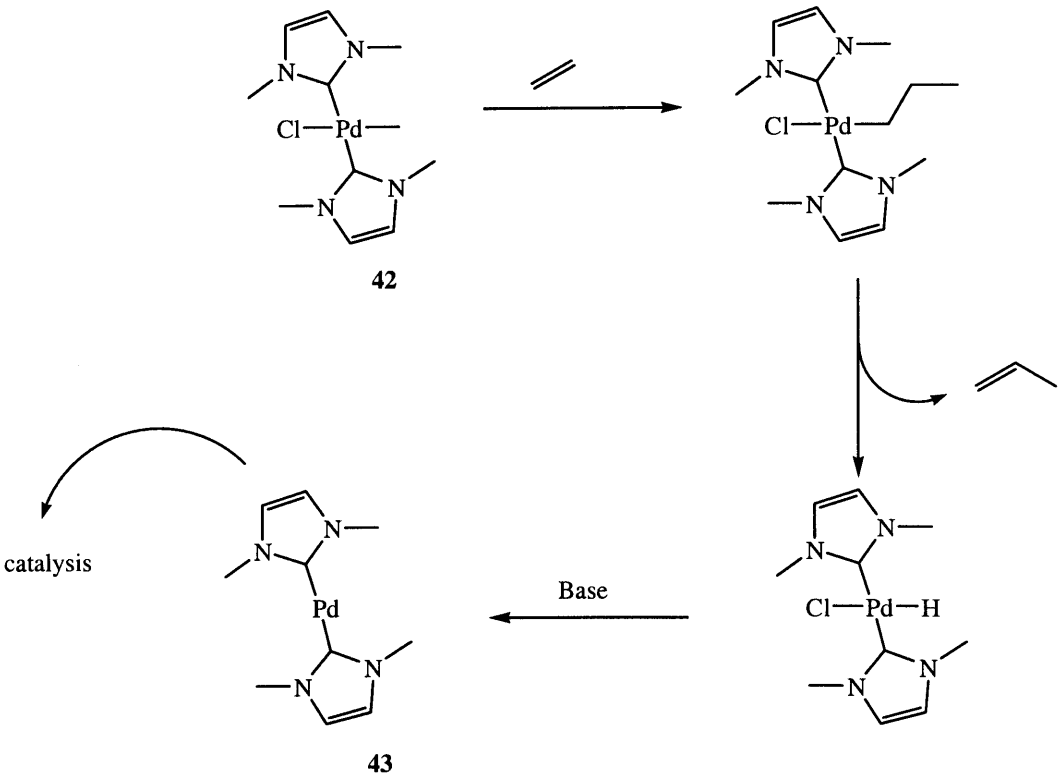
Application of this reactivity, to the task of oxidising methane was demonstrated, and a TON of 30 reached in 14 hours at 90 °C and an initial methane pressure of 30 bar.[117]
As a consequence of their high thermal stability pincer based NHC palladium complexes have given some of the highest turnover numbers yet reported for Heck cross coupling reactions using aryl chlorides, and a TON of 75,000 at 165 °C was achieved in 20 hours between styrene and 4-Chlorobenzaldehyde using complex **41**.[118]



41

Figure 19

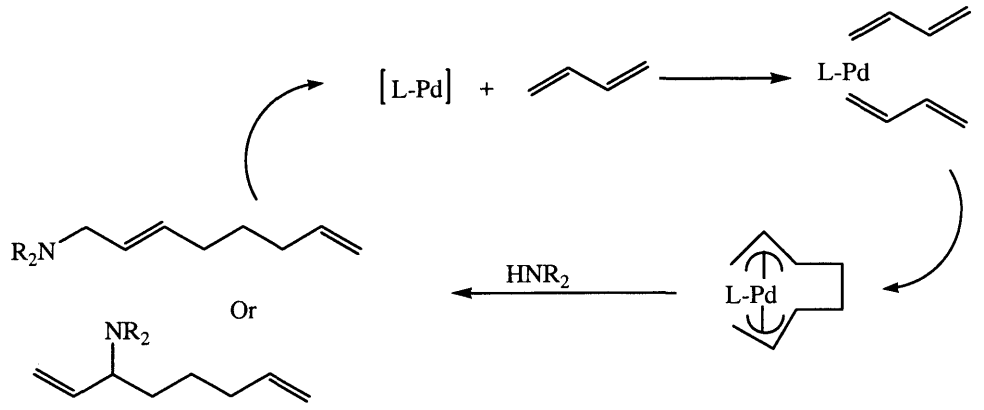
Methyl-palladium-NHC complexes are among the most active catalysts available for Heck type olefinations of aryl rings. This is in part due to the facile formation of a Pd (0) species, and also due to the stabilising effects of the NHC ligands.[8c] This stabilisation of the Pd (0) is imparted by the steric bulk of the ligand, with its strong electron donation properties also preventing ligand dissociation and eventual deposition of elemental palladium.



Scheme 12

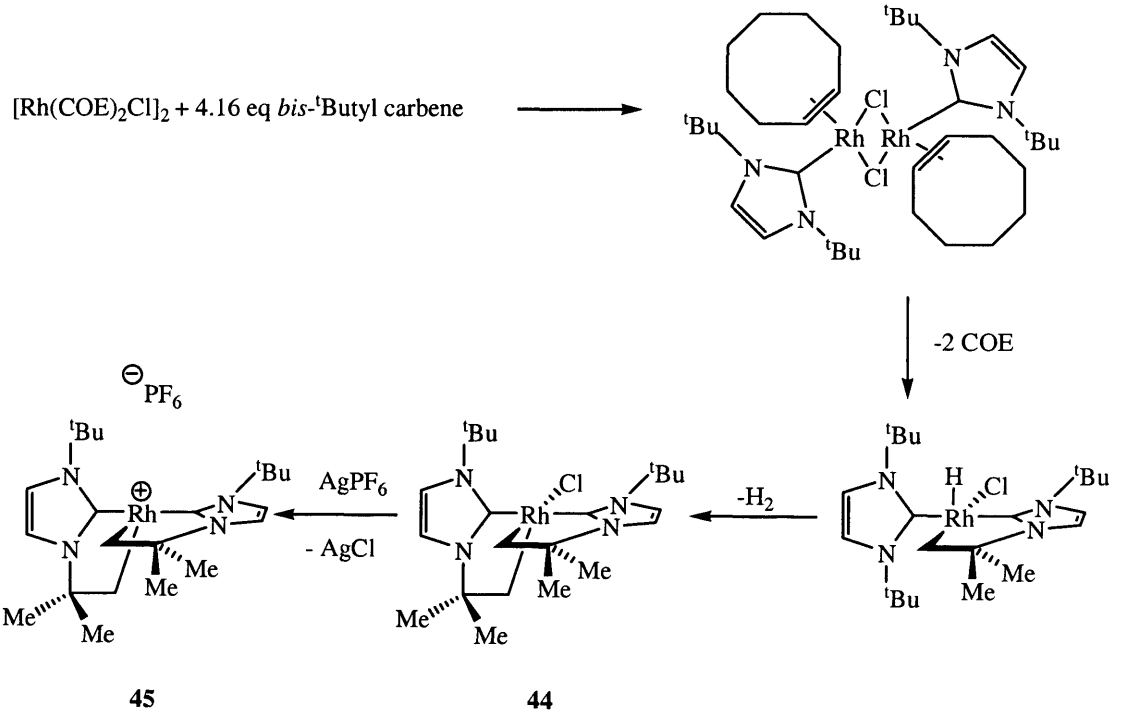
When complex **42** is used to affect the coupling of *n*-butylacrylate and 4-bromoacetophenone, a rapid and quantitative yield of product is achieved in 25 minutes, demonstrating TON's of up to 24,000.[8c]

Cationic NHC complexes of palladium promote the rapid and selective combination of 1,3-butadiene and an amine into telomers. The active complexes are conveniently prepared *in situ* and display good activity even at very low catalyst loadings (0.2mol%). Operating temperatures are mild and can be as low as room temperature. Both secondary and primary amines are cleanly converted to the corresponding telomers, Scheme 13.[119]



Scheme 13

The added stabilisation provided by NHC ligands has allowed for the detection and study of many reactive organometallic intermediates that have never been fully characterized in analogous phosphane chemistry, even despite the use of sterically demanding phosphine ligands. Examples are the double C-H activation of a Rh-NHC complex (i.e. **44**) with isolation of the 14-electron Rh (III) complex **45** facilitated by removal of the chloride using a silver cation (Scheme 14).

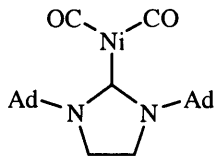


45 **44**

Scheme 14

Activation of C-H bonds by Rh (III) is extremely uncommon, and double cyclometallations of ligand systems on rhodium were previously unknown.[120] Saturation of the vacant sites in the 16- (**44**) and 14-electron (**45**) complexes with carbon monoxide gave the ability to conduct structural comparisons. DFT calculations show that these electrophilic metal centres are stabilized by π-donation of the NHC ligands.[121]

Similarly, whilst four-coordinate NiL_4 complexes are well known from the work of Tolman with phosphine ligands, a stable, three-coordinate $Ni(CO)_2(NHC)$ complex **46** has recently been isolated and characterised. Three coordinate Nickel species are exceeding rare in the literature. Insights into the strength of the Ni-NHC bond were also gained via calculations based on data for this compound.[122]



46

Figure 20

1.7 Conclusions

The foregoing review has hopefully indicated that NHC-metal complexes have become widely accepted as useful ligands in a broad spectrum of organic transformations. No longer should they be referred to as phosphine mimics, as they have been shown, in their own right, to have many applications where they are more active and efficient than phosphines, offering different reactivity profiles and even supporting new reactions not seen with the associated phosphine complexes. The ease of preparation of the more common ligand precursors, their air and moisture tolerance, as well as their greater basicity in comparison to many tertiary phosphines make NHC ligands superior in many cases to phosphines. The greater stability imparted to the metal complex by NHC ligands *vs.* phosphine ligands helps prevent catalyst degradation and elemental metal aggregation, thereby prolonging catalyst lifetime. The generally accepted non-dissociative nature of the NHC ligand with the metal eliminates the need to add excess ligand to the reaction mixture,[123] with obvious advantages, not least the fact that many ligands used in catalysis are more expensive than the transition metal being employed.

Chapter 2

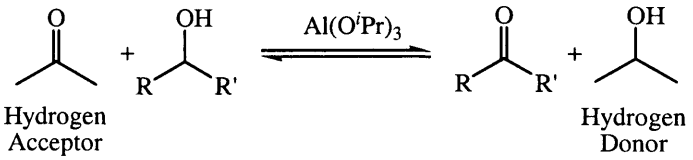
Hydrogen Transfer Reactions

2.0 Transfer Hydrogenation / Oxidation Overview

Oxidation and reduction are two of the most fundamental operations in organic chemistry. Lavoisier's original definition of oxidation was that a substrate should gain oxygen and/or undergo the loss of hydrogen and the reverse of this statement is how we could define reduction.

Although oxidation and reduction are generally considered non-reversible processes, under certain conditions, however this is not the case. The classical Meerwein-Ponndorf-Verley[124] (MPV) reduction utilises an Al catalyst that is capable of facilitating the reduction of substrates *via* the transfer of hydrogen from a 'hydrogen donor' to a substrate - the 'hydrogen acceptor'. An extension of this methodology is the Oppenauer oxidation,[125] in which Oppenauer recognised the reversible nature of the system (Scheme 15) and oxidised substrates under similar conditions to those which had been previously used for reduction. Both of these reactions rely on the differing oxidation potentials[126] of the carbonyl moieties when exposed to the reaction conditions, to favour formation of product, as well as employing a large excess of the hydrogen donor to help drive the equilibrium in the desired direction.

Oppenauer oxidation



Meerwein-Ponndorf-Verley Reduction

Scheme 15

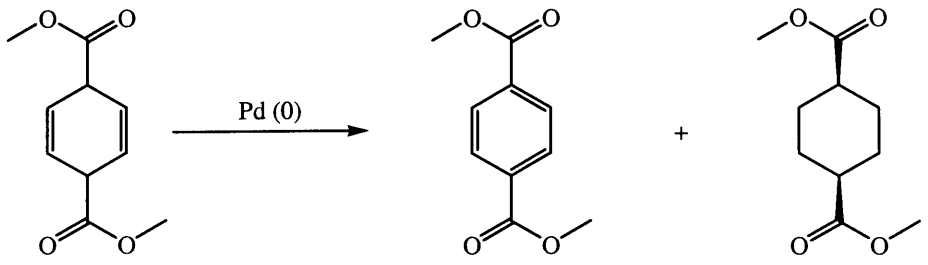
MPV-O based reactions are continually being studied and improved,[127] with new catalysts such as borinic acid derivatives,[128] magnesium phosphates,[129] Ir,[130] Rh[131] and Cr[132] complexes, all recently being published, as well as a non-catalytic supercritical variant.[133]

A process whereby hydrogen is *transferred* from one molecule to another is known as a hydrogen transfer reaction. This term is used in its broadest sense to include both intra-

and intermolecular interactions between organic compounds in which covalently bound hydrogen atoms change their site of attachment. These types of reaction are seen in many areas of organic chemistry and in biological systems, including thermal processes such as dehydrogenation of organic molecules in the presence of suitable acceptors, homogenously catalysed transformations such as the oxidation-reduction of alcohol-carbonyl based moieties, as well as heterogeneously catalysed conversions such as those that occur on the surface of various transition metals. Also in this group of reactions, we can include a multitude of photochemical reactions, the most widely known of which is, of course, photosynthesis.

A subgroup of hydrogen transfer reactions is transfer hydrogenation. This is the reduction of an organic substrate by the transfer of a H_2 equivalent from a suitable donor molecule. The importance of transfer hydrogenation stems from its ability to reduce molecules without the need for high pressures of flammable hydrogen, which is a prerequisite for the traditional methods of catalytic reduction. In fact, transfer hydrogenation does not even use molecular hydrogen. This is of particular importance when the reaction is to be carried out on a large scale, where significant quantities of the low atomic mass, and therefore highly diffusible hydrogen is usually required to be stored, transferred and reacted, all under pressure. Transfer hydrogenation removes many of the difficulties associated with performing hydrogenations, as no gas is required and the experimental set up is very simple with the entire process being carried out at atmospheric pressure. Alternative methods of hydrogenation, apart from transfer hydrogenation and homogenous or heterogeneous catalytic hydrogenation using molecular hydrogen, include reduction by metal hydrides,[134] radical addition of hydrogen atoms, and finally, electron transfer from either an electropositive metal, or *via* electrolysis, followed by proton quenching.[135]

In 1903, Knoevenagel[136] observed that dimethyl 1,4-dihydroterephthalate **47** disproportionated readily in the presence of elemental Pd (0) to give dimethyl 1,4-terephthalate **48** and predominantly *cis*- dimethyl 1,4-hexahydroterephthalate **49**, Scheme 16.

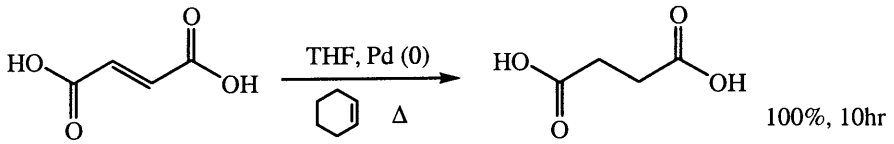


47 48 49

Scheme 16

The work by Knoevenagel was complemented by a similar series of experiments carried out by Wieland[137] in 1912. This work revealed similar results when using dihydronaphthalene as the substrate. Due to the low yields, long reaction times, and limited scope of substrates, this reaction was not further developed.[138] Encouraging results were later published when Zeliniski[139] and Corson[140] confirmed the predictions of Wieland that dihydrobenzenes would also undergo the disproportionation reaction which he had observed. Wieland had been unable to complete this work himself, as at the time he had no means by which to synthesise the required unknown precursors. Another reason for the lack of interest in transfer hydrogenation was that molecular hydrogen and hydrides were being very successfully applied at that time to the reduction of organic species. Reductions using molecular hydrogen were based almost exclusively on heterogeneous catalysis using Ni, Pd and PtO_2. Rylander and Bartók have both independently reviewed the field of heterogeneously catalysed reductions.[141]

Despite the general lack of interest in transfer hydrogenation Linstead worked on improving the earlier research. He published results in 1952 that for the first time showed this reaction to be a useful and viable method by which a range of substrates could be reduced under facile conditions.[142] Using Pd (0) in refluxing THF, substrates could be reduced in the presence of cyclohexene. Double and triple bonds, aliphatic and aromatic nitro groups, azo, azoxy and azomethine functionalities as well as halides, could all be reduced in high yields and purities (Scheme 17). Kindler improved this methodology further in 1966.[143]



fumaric acid succinic acid

Scheme 17

Braude and Linstead recognised three different possible transfer hydrogenation reactions:[144]

1. Hydrogen migrations. These take place on an intramolecular level.
2. Hydrogen disproportionation. The transfer of hydrogen in an intermolecular mode between two identical donor-acceptor units.
3. Transfer hydrogenation-dehydrogenation. This reaction occurs between two non-identical donor-acceptor molecules.

These three classes of reaction can be initiated *via* thermal means, homogeneous or heterogeneous catalysis, photochemically or with the aid of biological processes.

With the publication of Linstead's results, transfer hydrogenation became a valuable technique and a surge of research activity has ensured its continued success.[138, 145] Early work used unsaturated terpenes, hydroaromatics or alcohols as the hydrogen donors and a wide variety of organic substrates as the hydrogen acceptor. Many further donors, including formic acid and formates, (tetraethyl ammonium formate, TEAF, is used in organic systems),[146] phosphinic acid and phosphinates, hydrides of boron, aluminium, silicon and tin, alcohols, and hydrocarbons,[138] have all been demonstrated to be successful, as has hydrazine.[147] An important advantage can be harnessed if the hydrogen donor decomposes after donation of 'H_2' to give products with a large negative enthalpy of formation. Hence, CO_2 from formic acid and N_2 from hydrazine result in the reaction reaching completion in a faster time than one might otherwise expect. A similarly broad range of hydrogen acceptors has been catalogued, including ketones, α β-unsaturated carbonyl compounds, imines, epoxides and nitro groups. One paper even demonstrates the use of benzene as the hydrogen acceptor, albeit under forcing reaction conditions (>300°C).[148]

Hydrogen transfer is a thermodynamically driven process, with the implication therefore that the reaction will stop when an equilibrium point has been established. Judicious selection of hydrogen donor and acceptor must be made to ensure the reaction goes to completion. Use of a donor with a significantly lower oxidation potential than that of the acceptor will favourably affect the point of equilibrium, until the reaction becomes effectively under kinetic control as implied by Table 1, which shows the oxidation potentials of some representative carbonyl species.[126]

Carbonyl species	Oxidation Potential (mV)
2-Cyclohexanone	85
3-Pentanone	110
Propyl phenyl ketone	113
Acetophenone	118
2-Butanone	123
Cyclopentanone	123
iso-Propyl Phenyl ketone	123
Acetone	129
Benzophenone	129
Cyclohexanone	162
Tert-butyl phenyl ketone	169
Cinnamaldehyde	186
Benzaldehyde	197
2-Methyl propanone	220
Formaldehyde	257

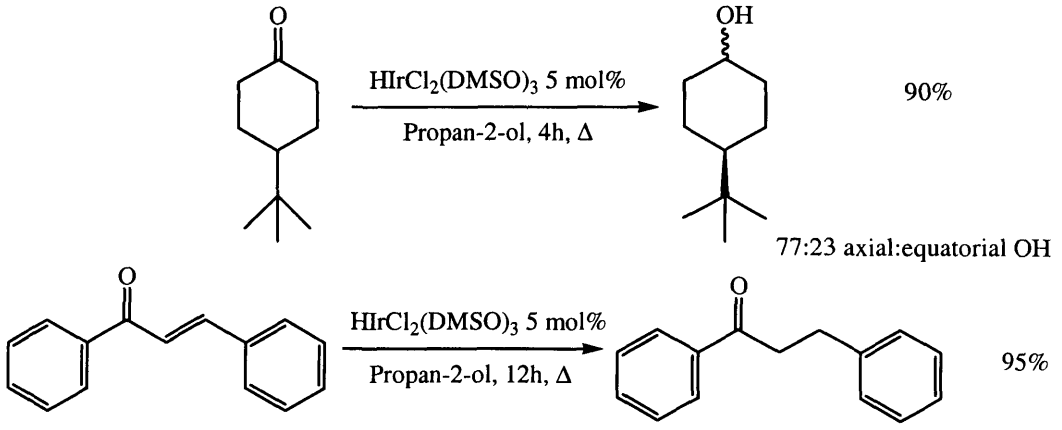
Table 1

The most commonly used transfer hydrogenation donor is propan-2-ol, as it is cheap, non-toxic, and volatile as well as being a good solvent. Its dehydrogenated product, acetone, is relatively unreactive, environmentally benign and easily removed from the reaction system.

The application of $Al(O^iPr)_3$ as a catalyst in hydrogen transfer reactions has many of the usual problems of a heterogeneous catalyst associated with it. Thus, long reaction times, 40 – 100 hours being usual, and elevated temperatures,[142] have disfavoured the use of this catalyst, especially should sensitive substrates be involved.

A significant development in the practical application of transfer hydrogenation was made when Henbest[149] and Hatani[150] developed the first homogenous catalysts for the reaction. This work evolved from the discovery that molecular hydrogenation could be catalysed *via* homogeneous catalysis using almost all of the group 8 transition metals.[151a] The most significant catalyst in this movement from hetero- to homogenously promoted reactions is undoubtedly $RhCl(PPh_3)_3$, Wilkinson's catalyst,[152] an easily prepared, air-stable Rh (I) complex which has become established as a standard hydrogenation catalyst.[151b]

Henbest developed an Ir based catalyst, $HIrCl_2(DMSO)$, with which he demonstrated the reduction of ketones and α, β-unsaturated ketones in high yield, using propan-2-ol as both the solvent and hydrogen donor (Scheme 18).[149]

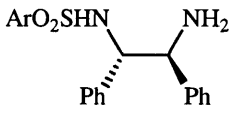


Scheme 18

Heterogeneous catalysts possess many advantages over their homogeneous counterparts, although one particular 'advantage', the ease of workup, can just as easily become a disadvantage.[151b] The work up of a heterogeneous hydrogenation generally involves simple removal of the catalyst from the reaction solution *via* filtration, but this simplicity is marred by the fact that the then dry catalyst may catalyse the combustion

of hydrogen or organic vapours with obvious safety implications. A homogenous catalyst has 100% of its active sites exposed to the reaction substrates allowing for very efficient and rapid reactions compared to the very limited amount of active sites available with an insoluble catalyst. Diffusion of both heat and mass are of critical importance to an inhomogeneous catalyst, but this is not an issue for an infinitely dispersed homogeneous catalyst. A further problem with an inhomogeneous catalytic species is the inherent irreproducibility of production. Since characterisation on a molecular level is exceedingly difficult, manufacturer and even batch-to-batch variability have a large effect on their reactivity,[153] leading to a general feeling of 'black box' chemistry and distrust of these catalysts.

Recent advances in homogeneous transfer hydrogenation catalysts have taken advantage of all the platinum group metals with ruthenium being the favoured choice. Further significant advances to the methodology have included asymmetric catalysts, offering high TOF's, TON's, ee's and yields, whilst remaining simple to prepare.[145, 154] Of particular note are the N-tosyl diamine ligands (e.g. **50**) of Noyori.[155] These ligands have provided the major advance in the application of Ru (II) mediated enantioselective reduction. Ketones are reduced to the corresponding alcohols in high chemical and optical purity, at room temperature using potassium isopropoxide as co-catalyst.



50

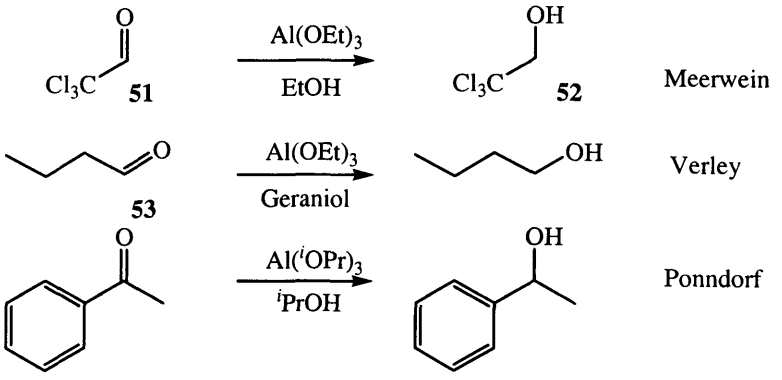
Figure 21

Asymmetric transfer hydrogenation is now a very competitive field, and as such, has been developed into a simple and versatile synthetic tool. The methodology permits the reduction of a wide variety of olefins and carbonyl groups, nitriles, nitro compounds, and other nitrogen containing unsaturated functional groups, as well as hydrogenolysis of benzylic and allylic functionalities and the replacement of aromatic halogens with a hydrogen atom. The donors are readily available, cheap organic compounds and the yields, in most cases, are excellent being fully comparable to those of traditional catalytic hydrogenation with H_2. The reaction is somewhat more selective

than regular hydrogenation because of the varying methods by which substrates can coordinate to the catalytic complexes and in special cases, such as the reduction of unsaturated steroids possessing several double bonds, has proven superior.[195] There is no question as to the greater experimental convenience of catalytic transfer hydrogenation, which avoids the use of the elaborate apparatus necessary for the high pressures required by traditional hydrogenation.

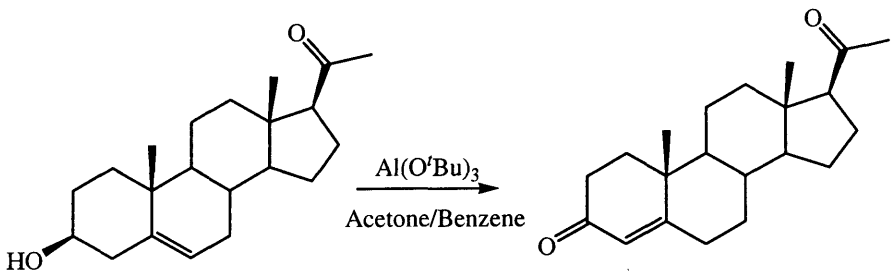
2.1 Non-Transition metal catalysed hydrogenation.

As previously mentioned, Meerwein discovered in 1925 that aluminium ethoxide is capable of transferring hydrogen from a hydrogen donor to a suitable substrate. In the original paper an example given was the clean reduction of chloral **51** to the corresponding alcohol **52** in ethanol. Further improvements to this initial offering, by Verley, demonstrated the reduction of butyraldehyde **53** using geraniol as the H-donor and by Ponndorf, who extended the scope of the reaction to include ketones, resulted in a general and practical method for the reduction of carbonyl substrates in the presence of alcohols, without the need for hydrogen gas (Scheme 19).



Scheme 19

It took 12 years until the reversible nature of this reaction was taken advantage of by Oppenauer, who published conditions whereby alcohols can be oxidised to the corresponding carbonyl analogue in the presence of a hydrogen acceptor,[125a] using aluminium *tert*-butoxide as the optimal catalyst. An example of this new oxidation is the conversion of progesterol **54** to progesterone **55**, Scheme 20. This oxidation showed promise due to its mild nature and high yields, making it ideal for more complex natural product synthesis. A second and incredibly useful feature of the Oppenauer oxidation is that over oxidation to the carboxylic acid is not possible.

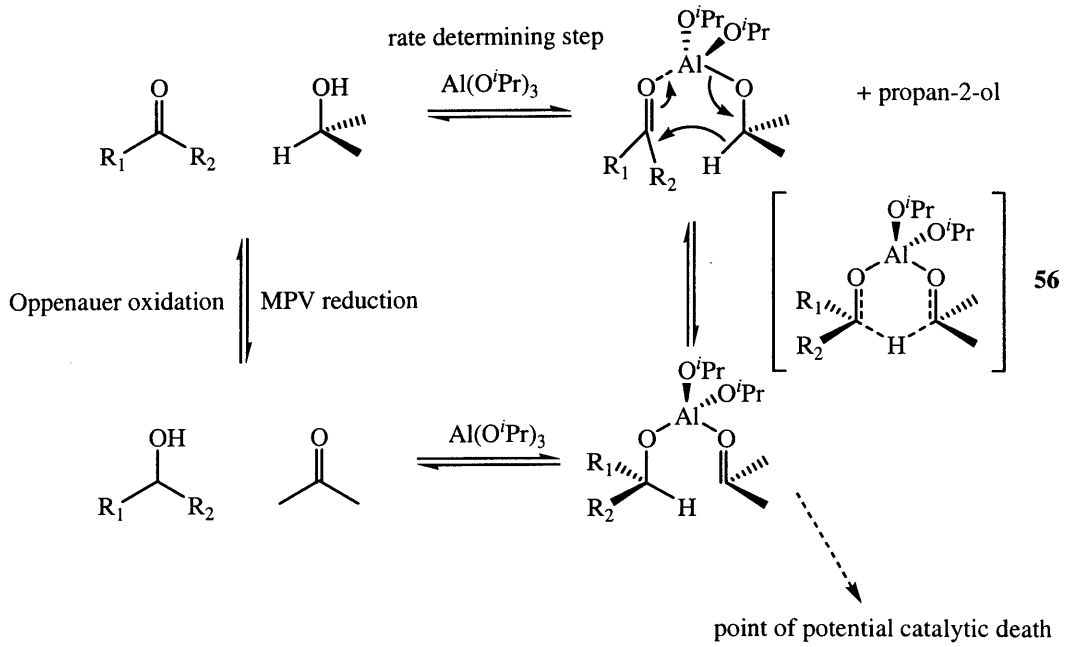


54 **55**

Scheme 20

By controlling the reaction conditions it is simple to manipulate the equilibrium to give either alcohol or carbonyl product without effecting neighbouring functional groups. There have been several reviews on the topic of hydrogen transfer as applied by Meerwein, Ponndorf, Verley and Oppenauer. Djerassi[125b] and Wilds[125b] discussed the developments in the pre-1950 literature, whilst Huskens[156] has focused on the more recent literature. A review by Lehmann[157] has brought together the literature relating to the Oppenauer oxidation with specific sections on reactions involving steroids and the more problematic alcohols containing nitrogen functionality.

The mechanism of the MPV reaction has been firmly established and is considered a hydride shift in equilibrium.[125b, 156, 158] An initial complex between the carbonyl moiety, the reducing alcohol, in the form of its alkoxide, and the Al centre is formed (Scheme 21).



Scheme 21

Once the carbonyl has coordinated to the Al (III) centre, it becomes activated towards nucleophilic attack, since the Al atom acts as a Lewis acid. A hydride is transferred from the coordinated alkoxide to the carbonyl group *via* a six-membered transition state **56**.[159] The Al also acts as a tether to hold the reactants in close proximity in order to facilitate the hydride transfer step. The newly formed alkoxide is released from the metal complex by alcoholysis, during which a proton is abstracted from the bulk solvent, quenching the newly liberated product alkoxide, thereby completing the cycle. It has been shown by Shiner[158b] that the rate determining step in this process is not, as once believed,[160] the hydride transfer step, but rather the alcoholysis/proton abstraction step. This rate is further retarded should the metal have a greater affinity for the newly formed alcohol than for the reactant. The slow exchange of a 'product alkoxide' for a 'donor alkoxide' results in catalyst deactivation, and it is often for this reason that stoichiometric amounts of 'catalyst' are used. This mechanism is often referred to as the *direct hydrogen transfer* mechanism. Direct proof for a hydride shift was demonstrated by a deuterium tracer study using 2-deutero-2-propanol.[161] Doering published evidence that eliminated a possible radical mechanism.[162]

When Lehmann wrote his review in 1975, he emphasised work done in the area of MPV reaction on nitrogen substituted alcohols. The reason for this is that the number of

successful MPV-O reactions done on compounds containing basic nitrogen atoms was minimal, due to rapid deactivation of the metal catalyst.[163] This deactivation of the Al based catalysts results from the stable complexes that are formed between the basic nitrogen lone pair and the 6-electron Al (III) species. The commonly observed precipitate in this troublesome reaction is most likely the $R_3Al^-:{}^+NR_2$ adduct. Various techniques were tried to overcome this problem, such as forming a salt of the substrate to suppress the basicity of the nitrogen lone pair, but usually to no avail. Woodward managed to circumvent these problems, demonstrating his ability to see alternative solutions to otherwise seemingly complex problems. The role of the Al complex is to activate the carbonyl compound, thereby facilitating the hydride transfer from the donor. This 'push-pull' activation method is also seen, but to a lesser extent, if one uses a metal alkoxide other than Al,[158] as demonstrated in Figure 22.

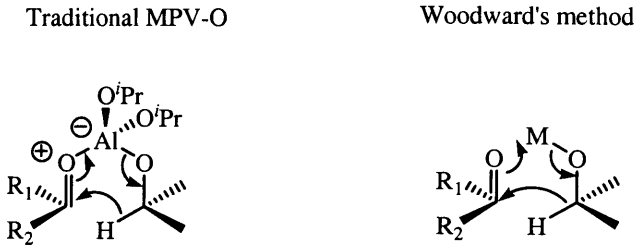
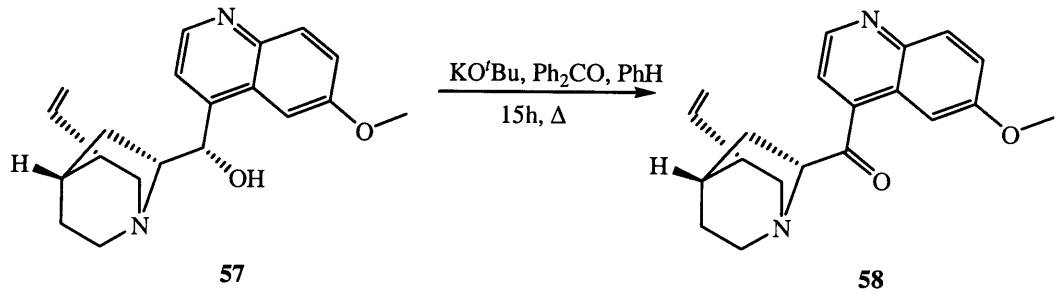


Figure 22

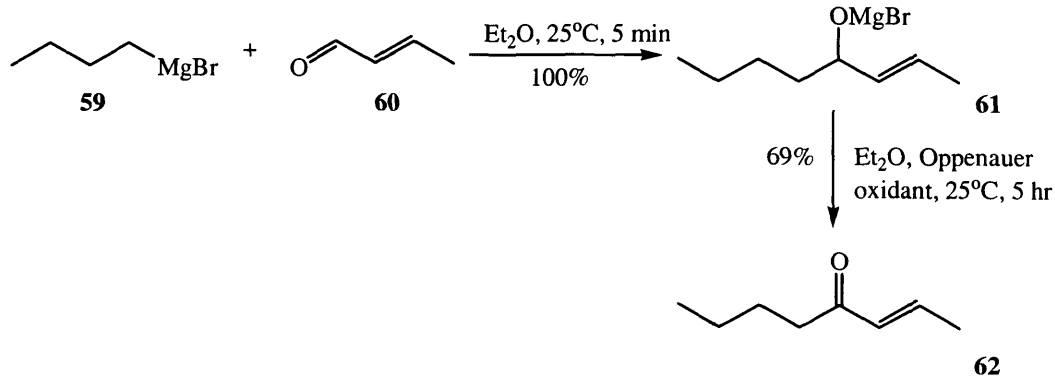
Potassium *tert*-butoxide proved to be an excellent mediator for Woodward's modified MPV-O reaction and quinine **57** was oxidised to quininone **58** using benzophenone as the hydrogen acceptor in 95% yield.



57 **58**

Scheme 22

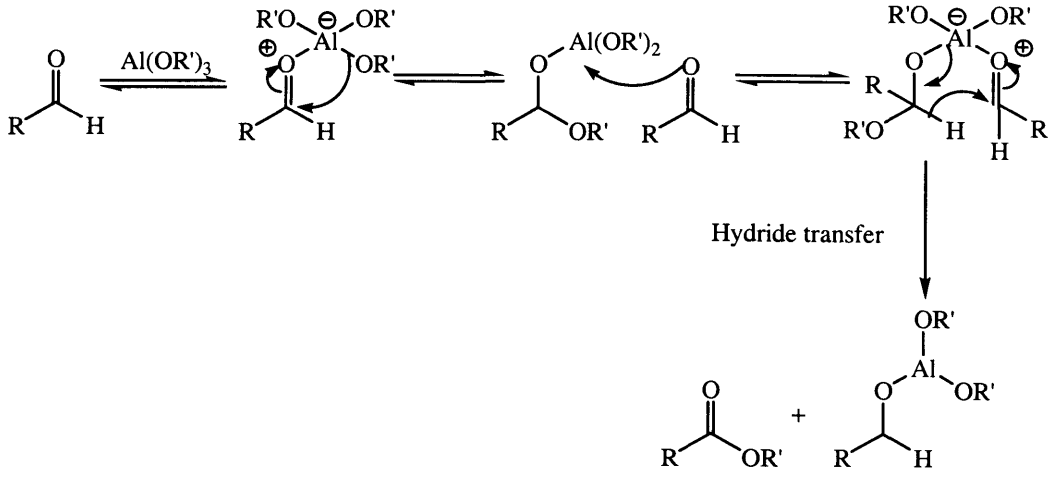
Under similar alkaline conditions, the reaction can be pushed in the opposite direction, resulting in reduction. When quininone **58** was heated for six hours in toluene with 10 mol % of sodium isopropoxide, quinine **57** and quinidine were formed in yields of 30 and 60 % respectively. This reaction was for several years believed to proceed by a direct hydride transfer mechanism as indicated in Figure 22, but recently it was shown more likely to proceed *via* a single electron reduction mechanism instead of by direct hydride transfer.[159,164] A more recent example of this modified Oppenauer type reaction is seen in the work of Byrne, who used a Grignard reagent in a one-pot alkylation-oxidation reaction, Scheme 23.[165] The first step uses a classical Grignard reaction between *n*-butyl Magnesium bromide **59** and crotonaldehyde **60**. The resultant magnesium alkoxide **61** is then stirred with an Oppenauer type oxidant to yield the ketone **62**. In this case, the Mg atom acts as the Lewis acid *via* a Woodward type MPV-O mechanism. Suitable oxidants were benzaldehyde, chloral and furfural. Critical for a successful reaction is that only weakly or non-coordinating solvents such as diethyl- or diisopropyl-ether could be used. When solvents such as THF were used, the reaction failed.



Scheme 23

Although MPV-O type reactions are tolerant to many functional groups, several problems have been documented such as the reduction of compounds which require mild conditions to avoid degradation. An example of the effect of temperature and solvent on the MPV-O reduction of aromatic dinitro compounds using hydrazine as the donor, in ethanol as solvent, was published by Bond and Wells.[166] Between 25-30 °C, no reduction was observed but reduction was fast at 78 °C. Addition of DCM to the ethanolic reaction solution resulted in reduction occurring at 28°C, yet on raising the temperature to 78 °C many side-reactions occurred, with the formation of tar-like

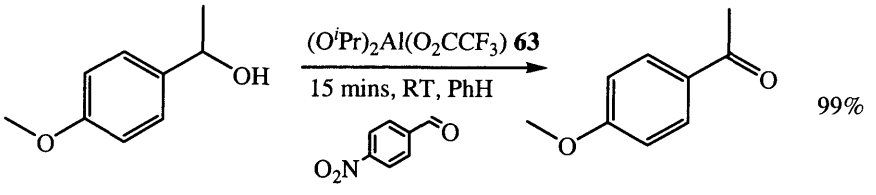
products. The role of DCM in this process was not fully understood, but may be related to the extent of aggregation and/or dispersion of the catalyst. For some hydrogen donors, increases in reaction temperature increase the rate of decomposition of the donor without an equivalent increase in the rate of reduction of the hydrogen acceptor.[167] Another common, and often detrimental side reaction associated with transfer hydrogenation, is the aldol condensation. Aluminium alkoxides are very good catalysts for aldol reactions and problems can occur when aldehydes are present in the starting material or are formed during the reaction, as is the case with the oxidation of 1° alcohols. The aldol product can also subsequently dehydrate and the resultant water quenches the catalytic alkoxide species. If the aldol condensation is not an issue, for example in compounds that do not posses a suitable enolisable proton, e.g. benzaldehyde, the possibility for a Tishchenko[168] reaction may arise, which results in disproportionation of an aldehyde to an ester and an alcohol molecule, Scheme 24.



Scheme 24

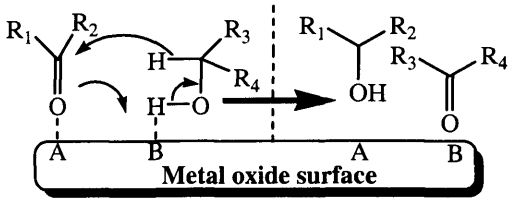
A further problem associated with the MPV-O is the poor solubility of aluminium alkoxides in the non-polar solvents usually applied to the reaction.[169] This affects the reproducibility of the reaction and is exacerbated by the tendency of the Al complexes to form oligomers,[170] thereby further reducing the solubility of the catalyst. The requirement for stoichiometric amounts of catalyst for satisfactory results in the MPV-O reactions, coupled with the development of metal hydride reducing agents such as $LiAlH_4$ and $NaBH_4$ in the 1950's and selective sub-stoichiometric oxidants resulted in advances in MPV-O type reactions losing their impetus until the 1980's.

Since that time, research has been directed towards improving the MPV-O group of reactions with the aim being to find cheap, environmentally friendly transformations that are chemoselective, operate under mild reaction conditions and are readily adaptable for both laboratory and large-scale synthesis. One such advancement has been a method to overcome the oligomeric, insoluble nature of the simple Al-alkoxide catalysts. The Nguyen group demonstrated the *in situ* formation of an Al-alkoxide from trialkyl-aluminium reagents,[169] which results in a much more soluble, low aggregation catalyst. Metal alkoxide bonds are highly ionic in character, and this property can be modulated depending on the groups attached to the alkoxide oxygen atom. The more electronegative the alkoxide, the easier it is for it to be replaced by another organic molecule, thereby increasing the TOF for the reaction. Coupled with this ligand exchangeability, lies a Lewis acidity character that varies extensively with the metal used, but which gives metal alkoxides their catalytic activity.[156] Finding the balance between these two properties is key to developing a successful catalyst. Aluminium alkoxides became the catalysts that are most commonly used in MPV-O transformations due to their easy preparation and wide availability. Aluminium (III) has a high charge density making it a very good Lewis acid, but as a result of this, it has relatively poor ligand exchange properties, which causes low turnover frequencies. The reaction rate can be accelerated by addition of protic acids such as trifluoroacetic acid, hydrochloric acid, propionic acid, or fluorosulphonic acid.[171] However, the rate acceleration from acid catalysis is often at the cost of yield since the aldol condensation is promoted under these conditions. An alternative method used to accelerate the reaction rate is to affect the rate at which ligand exchange can occur. Increasing the electronegativity of the alkoxide ligand is the most successful method to achieve this. Akamanchi demonstrated this by use of diisopropoxyaluminium trifluoroacetate **63** as the MPV-O catalyst and *p*-Nitrobenzaldehyde as the hydride acceptor, for the Oppenauer oxidation of a range of secondary alcohols (Scheme 25).[172]



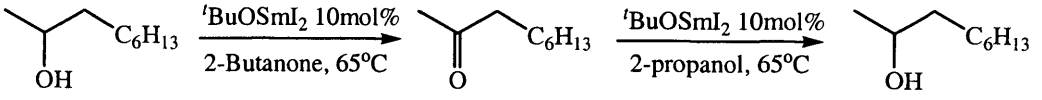
Scheme 25

Alteration of the ligand is not the only way to improve catalysis and Lanthanide oxides have been investigated as substitutes for Al.[173] These catalysts were shown to have two active centres, one basic and the other acidic (Scheme 26). The ketone is adsorbed on an acidic site (A) and an alcohol (hydrogen-donor) on an adjacent basic site (B), facilitating the transfer of a hydride. Many types of unsaturated ketones can be reduced to the corresponding unsaturated alcohols *via* this method. [138]



Scheme 26

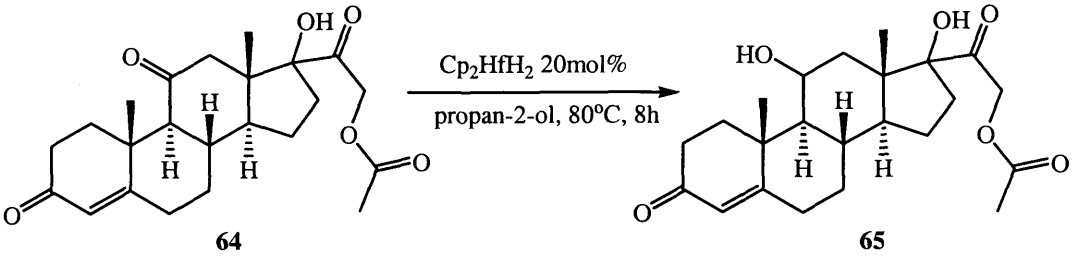
Since the 1980's, lanthanides have been gaining in popularity for organic synthesis, with substitution reactions, addition to carbon-nitrogen multiple bonds and carbonyl groups, nucleophilic acyl substitutions, reductive couplings, cyclopropanations and oxidative couplings being just a few examples of processes mediated by their presence.[174] Ln (III) ions show hard Lewis acidity, high ligand exchange rates and high coordination numbers, typically 8 or 9.[175] This combination of properties makes Ln (III) ions ideally suited to MPV-O chemistry. Namy was the first to apply lanthanide chemistry to MPV-O reactions,[176] oxidising and reducing an array of substrates using ^{t}BuOSmI$_2$ (Scheme 27). A collection of lanthanides was soon being applied to MPV-O chemistry, however there was no clear correlation between catalytic activity and the location of the particular metal in the lanthanide series.[177]



Scheme 27

Critical to any methodology is the ability to demonstrate chemoselectivity. Ishii used a hafnium[178] and a less active zirconium[179] catalyst to reduce polycarbonyl species to their

corresponding hydroxycarbonyl analogues, demonstrating selective reduction of one carbonyl group in the presence of another. This chemoselectivity has been demonstrated by the reduction of trione **64**, a steroid with 4 carbonyl groups, being reduced cleanly to dione **65**, in a respectable yield of 44% (Scheme 28).

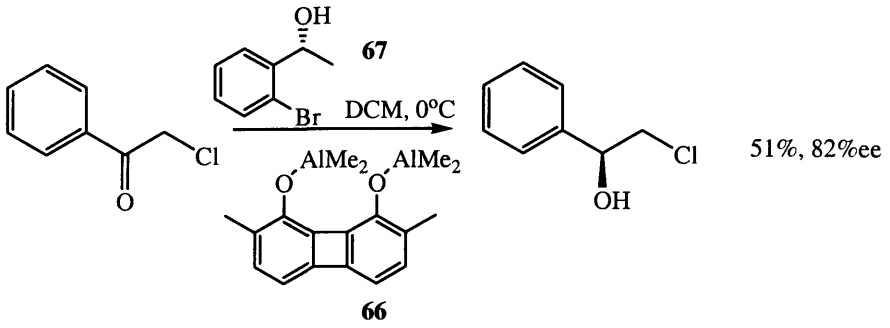


64 **65**

Scheme 28

Ishii's paper disclosing the zirconium mediated selective oxidation of diols contained examples showing that either hydroxy aldehydes or hydroxy ketones could be accessed *via* this truly 'catalytic' catalyst using only 10 mol% of complex, and they could also be re-used without noticeable lack of activity.

Further developments in MPV methodology incorporated asymmetry into the scope of the reaction. Initially asymmetry was achieved using optically active alcohols. Doering achieved an enantiomeric excess (e.e.) of only 22% in the reduction of simple ketones using (S)-(+)-2-butanol as the hydride source and aluminium 2-butoxide as the catalyst.[180] Independent attempts by Yamashita,[181] and Menicagli,[182] using chiral aluminium alkoxides, also achieved mediocre results. Intramolecular asymmetric MPV reductions have been achieved using chiral starting materials or chiral auxiliaries. Marouka developed a bidentate aluminium catalyst **66** that when used in conjunction with a chiral alcohol, (R)-(+)-*sec-o*-bromophenethyl alcohol **67**, gave reasonable yields (60-80%) and good ee's (70-80%) of the desired alcohols (Scheme 29).[183] A review article by Node details the state of the art of asymmetric MPV reactions.[184]



Scheme 29

Marouka's catalyst was one of the first examples of a well-defined, bidentate ligand and his catalyst **66** offered the possibility of double electrophilic activation.[185] Unlike standard MPV-O catalysts, where the aluminium alkoxides exist as oligomers in solution, the use of complexing multidentate ligands favours monomeric aluminium species, and offers outstanding activity for the rapid reduction of a range of substrates at room temperature, in high yield (Figure 23).

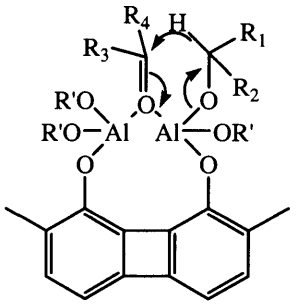
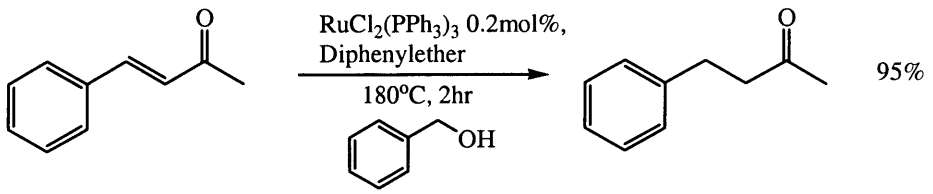


Figure 23

2.2 Transition metal catalysed transfer hydrogenation

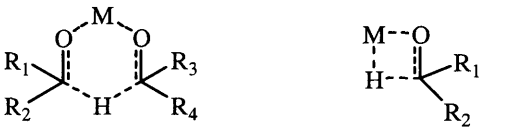
As we have already noted, Henbest, who applied an organo-iridium/propan-2-ol system to reduce ketones, was the first to use transition metals for transfer hydrogenation.[186] Bailar has utilised platinum complexes containing triphenylphosphine, -arsine, or –stibine in conjunction with either methanol or H_2 to also reduce a wide range of ketones.[187] Even with these discoveries, relatively little research was done in the field of transfer hydrogenation due to the wide success of homogeneously catalysed hydrogenation. This lack of interest in transfer hydrogenation was compounded by the relative lack of activity of catalysts, such as those of Henbest etc., and also due to the forcing conditions that were required in order to promote the reactions. Blum[188] for example used $RuCl_2(PPh_3)_2$[189] to reduce α,β-unsaturated ketones in diphenylether, using benzyl alcohol as the hydrogen source but required a temperature of 180°C (Scheme 30).



Scheme 30

The lack of activity of transfer hydrogenation catalysts for the reduction of alkenes or carbonyl functionalities was in sharp contrast to the activity of hydrogenation catalysts such as $RhCl(PPh_3)_3$, which is capable of reducing the unactivated alkene of hexene at room temperature rapidly and quantitatively at less than 1atm of hydrogen.[190] Many other early examples of incredibly facile hydrogenation by Wilkinson's catalyst ($RhCl(PPh_3)_3$) are present in the literature,[191] and it is easy to see why the application of transfer hydrogenation did not become widespread. However, discoveries of more active catalysts,[192] and more efficient hydride sources[193] were soon to make transfer hydrogenation a powerful tool. Phase transfer methodologies were also established so as these valuable metal species could be recovered and reused.[194]

During the late 1970's and 1980's it became apparent that there was more than one mechanism of reduction operating during transition metal catalysed transfer hydrogenation. A recent review by Morris[195] on the mechanism of transfer hydrogenation by Ru-hydride species collates the different mechanisms which have been observed. There are two general mechanisms, the direct hydrogen transfer mechanism, which proceeds *via* a 6 membered cyclic transition state, similar to that of the MPV reduction, and a hydridic route which proceeds *via* a 4 membered transition state, in which the substrate reacts directly with a metal hydride (Figure 24).



Direct hydrogen transfer Hydridic route

Figure 24

Bäckvall has contributed a considerable amount of research to establish the mechanism of the metal hydride type reaction, and *via* deuterium labelling has established that there is both a monohydride and dihydride mode of operation (Figure 25).[196]

Two divisions of the hydric route

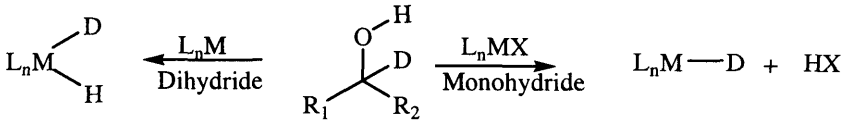


Figure 25

The two routes were distinguished by the observation that should the reaction be proceeding *via* a monohydride route, then the O-H proton and the C-H proton of the donor alcohol should be selectively transferred to the acceptor carbonyl functionality forming the new O-H and C-H bonds formed respectively. This is more easily understood by looking at Figure 26.[196b]

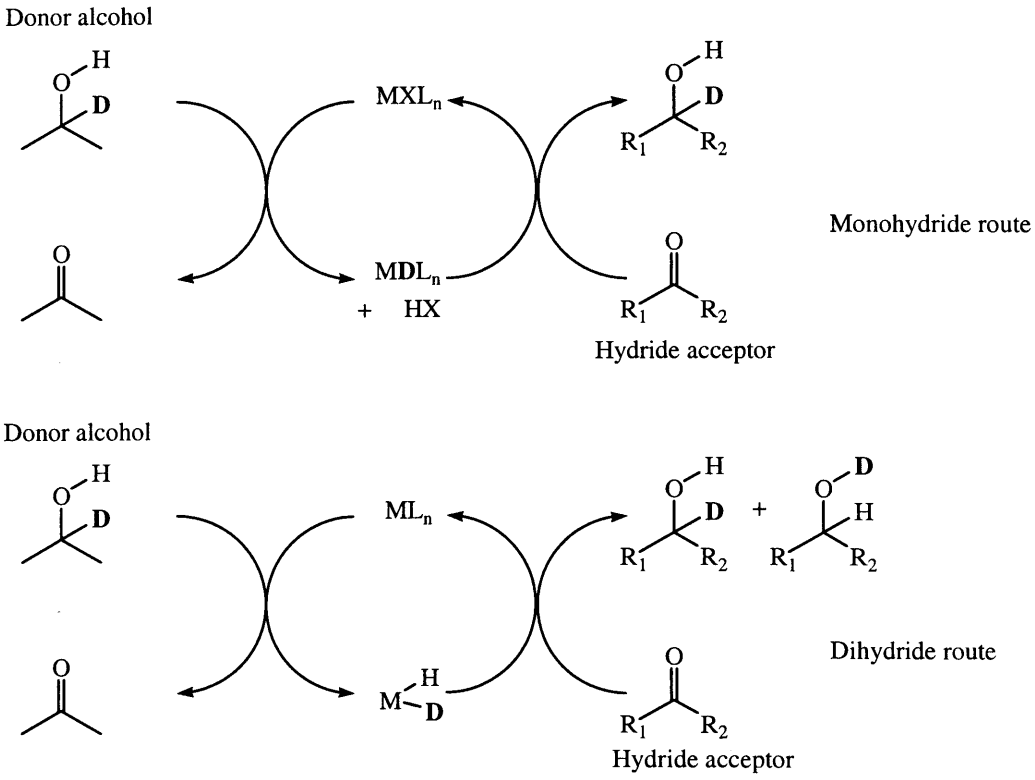
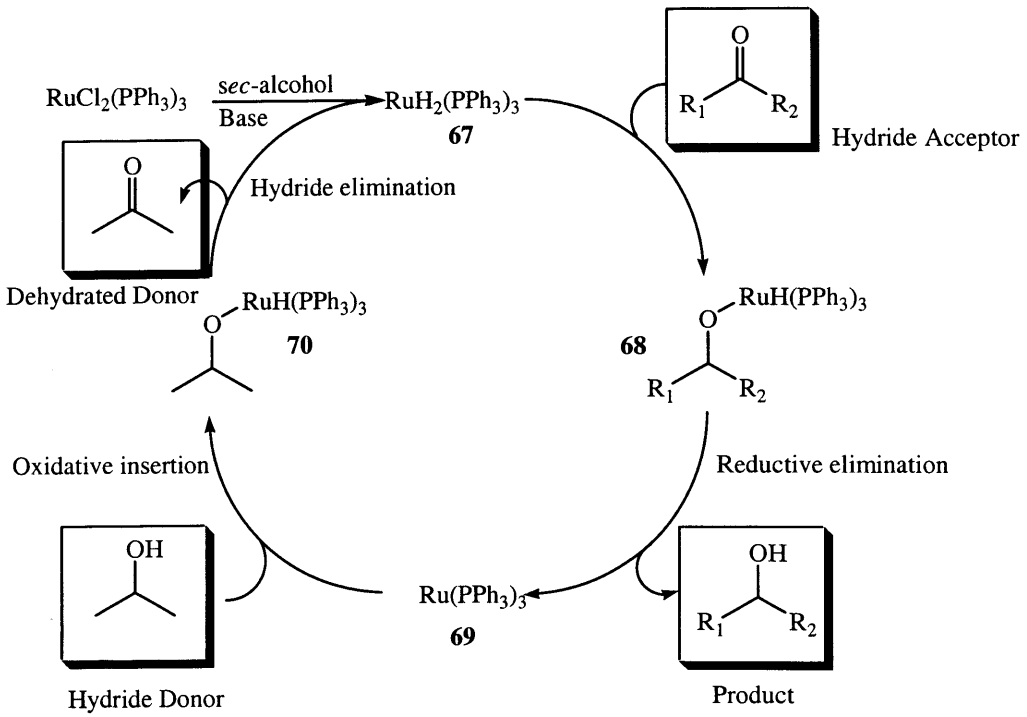


Figure 26

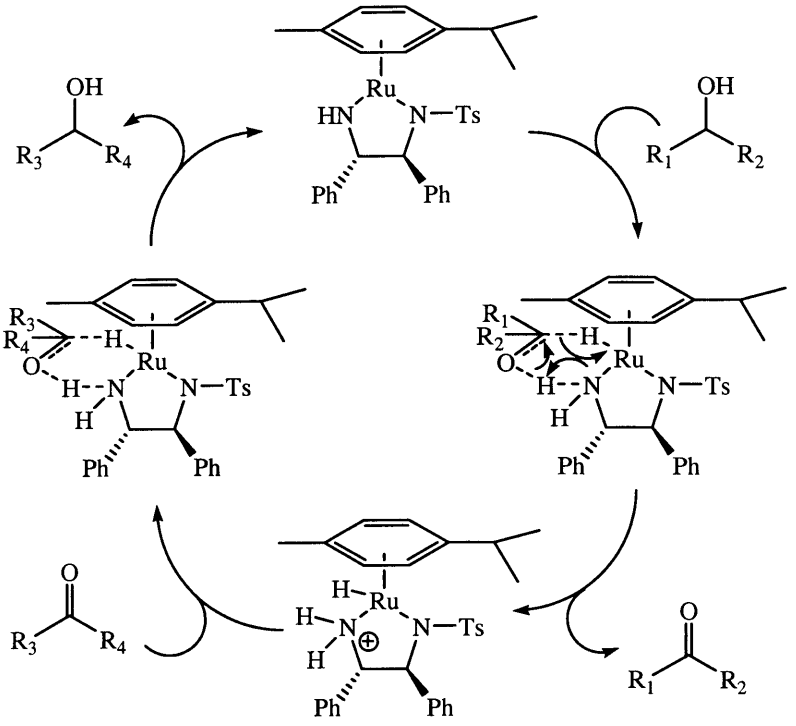
Should the mechanism follow a dihydride route, a statistical mixture of deutero-products will be formed. A direct hydrogen transfer mechanism, as occurs in a typical MPV reduction, proceeds with selective C-H to C-H migration. The studies performed by Bäckvall investigated ruthenium, rhodium and iridium with a selection of suitable ligands. He found that both rhodium and iridium catalysed reactions generally proceed *via* the monohydride route, whilst ruthenium is non-selective, catalysing the reaction *via* either mono- or di-hydride intermediates. A typical Ru catalysed (dihydride mechanism) as proposed by Bäckvall is detailed in Scheme 31.



Scheme 31

In-situ formation of the 16 electron Ru (II) species **67** is followed by coordination to the carbonyl substrate (hydrogen acceptor). This results in a hydride being delivered to the sp^2-carbon atom of the carbonyl group and formation of the intermediate Ru-alkoxide, **68**. Subsequent reductive elimination releases the product and delivers the Ru (0) species **69** that undergoes an oxidative insertion reaction with the hydride donor (e.g. propan-2-ol). The newly formed ruthenium-alkoxide **70**, *via* β-hydride elimination produces the dehydrogenated by-product of the reaction (in this case acetone), and, in the process, reforms the catalytically active 16-electron Ru (II) dihydride **67**.

As a consequence of his own work Noyori has discovered a third type of mechanism[197] to the previously established direct hydrogen transfer and hydride categories, termed metal-ligand bifunctional catalysis.[198] The origin of this name results from the active involvement of the ligand in the transfer of the hydrogen atom from the donor to the substituent.[199] The hydrogen atom is transferred as a hydride *via* a 6-membered transition state involving the simultaneous removal of the hydroxide proton by the amine of the ligand and a hydride by the ruthenium atom, from the substrate alcohol, Scheme 32.



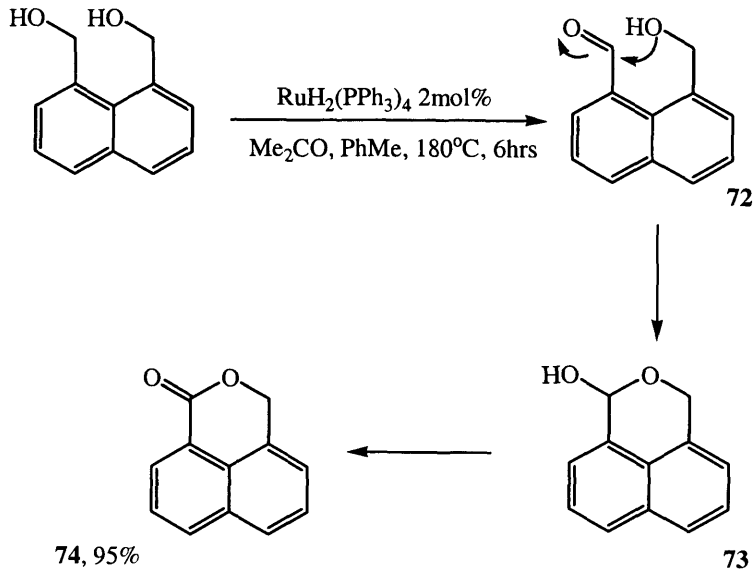
71

Scheme 32

This mechanism proceeds through a Ru-monohydride species **71**, which reduces the carbonyl substrate whilst the protonated ligand quenches the alkoxide to produce the alcohol. There have been several computational studies probing the mechanism of this direct transfer process and they concur with the mechanism outlined in Scheme 32.[200] Formation of the Ru-H species **71** by dehydrogenation of the donor alcohol has been shown to exhibit a double kinetic isotope effect, which would be consistent with the transfer of the two hydrogen atoms involved in the reductive process, and is believed to be the rate determining step of this mechanism.[201]

Along with the three discreet mechanisms mentioned previously, hydrogen transfer, metal-hydride and metal-ligand bifunctional; it is not unusual to see the same catalyst perform *via* differing mechanisms.[202] Sasson and Blum, in their pioneering investigation of $[RuCl_2(PPh_3)_3]$ catalysed H-transfer reactions, provided kinetic evidence for a direct hydrogen transfer in the reduction of activated carbon-carbon double bonds, whereas a hydridic mechanism was inferred for the transfer hydrogenation of saturated ketones.[188]

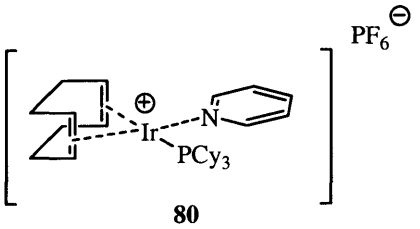
Investigations by Fukuzumi determined that Ru complexes such as $RuH_2(PPh_3)_4$, which is capable of alkene reduction, operates *via* the 14-electron species, $Ru(PPh_3)_3$, with the initial dehydrogenation of the alcohol to produce the Ru (0) species being the rate-limiting step.[203] All of the early Ru based systems suffered from the need for high temperatures (>180°C) and were of limited substrate scope.[204] The most troublesome substrates for hydrogen transfer catalysts are primary alcohols[205, 206] and this applies either to the dehydrogenation of a hydrogen donor for a MPV type reduction or to the Oppenauer oxidation of a primary alcohol to the corresponding aldehyde. An explanation for this lack of reactivity is the greater strength of the CH bond of primary alcohols in comparison to their secondary congeners. A second difficulty associated with the oxidation of primary alcohols is that the initially formed aldehyde **72** can react with a second molecule of the starting alcohol (either intra- or inter-molecularly) to form a hemiacetal **73**, which can be further oxidised to the ester **74** (Scheme 33). Although viewed as a common problem with many Ru based catalysts, e.g. $Ru_3(CO)_{12}$, $RuH_2(PPh_3)_4$ or $RuCl_2(PPh_3)_3$, it has also recently been recognised as a very powerful reaction in its own right. For example, the initially formed aldehyde **72** can be trapped by a variety of nucleophiles such as amines[207] and alcohols to afford useful products such as quinolines[207], indoles[208], amides[209] and lactones.[205b]



Scheme 33

2.2.1 Transition metal complexes bearing NHC ligands in hydrogenation

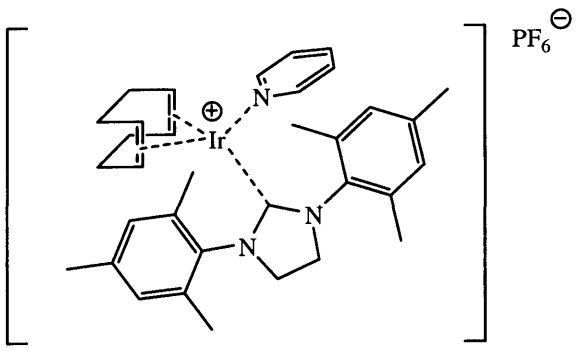
The most commonly used catalysts for homogenous hydrogenation include Wilkinson's catalyst ($RhCl(PPh_3)_3$) and Crabtree's catalyst ($Ir(COD)(py)(PCy_3)PF_6$) **80**.



80

Figure 27

Although these catalysts perform very well, they both degrade under the elevated reaction temperatures used for reactions.[210] Ruthenium and iridium based complexes containing NHC ligands have been applied to traditional hydrogenation reactions using gaseous H_2 for example the Ru complex $HRu(CO)Cl(PCy_3)$(1,3-bis-mesitylimidazol-2-ylidene) **81** has been shown to be active for the hydrogenation of alkenes under 4 atmospheres of hydrogen, yet at room temperature is not as active as the corresponding phosphine complex, $HRu(CO)Cl(PCy_3)_2$, **82**. With an increase in temperature however, the reactivity of the NHC complex **81** becomes more apparent. Thus at 100°C it has a TON of 24,000, slightly higher than that of the phosphine complex **82**, which exhibits a TON of 21,500.[211] Iridium catalysts tend to be more active than their Ru counterparts, and do not require such high temperatures or pressures of H_2 in order to achieve similar results. Replacement of the phosphine on Crabtree's catalyst **80** with the saturated carbene, 1,3-bis-mesityl-4,5-dihydroimidazol-2-ylidene produces a complex **83** that is also suitable for the hydrogenation of alkenes (Figure 28).



83

Figure 28

As with the ruthenium complex, the activity of the Ir-NHC functionalised complex is less active than the phosphine complex at room temperature. However, at 50°C, the NHC complex quantitatively reduces 1-methylcyclohexene to 1-methylcyclohexane, whilst the parent complex only achieves 34%.[212] A range of Ir catalysts (Figure 29) of general formula Ir(COD)(py)L where L is a NHC unit have been investigated for activity.

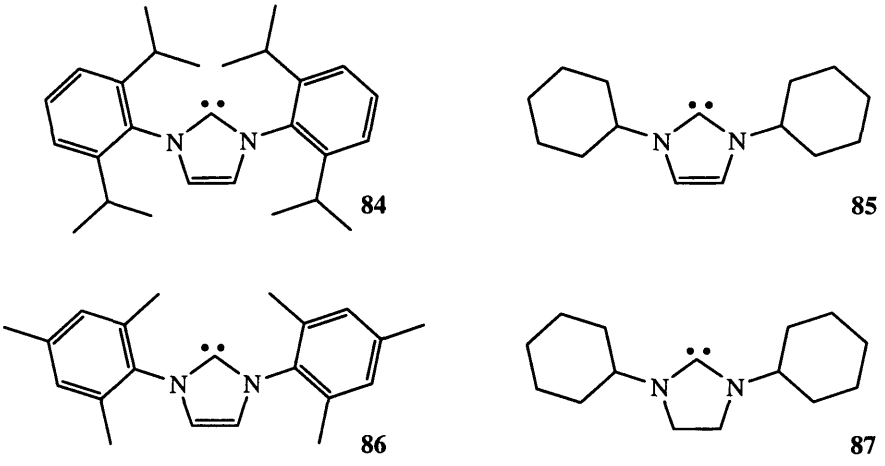


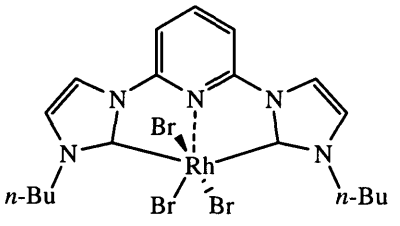
Figure 29

The complex bearing 1,3-bis(cyclohexyl)imidazol-2-ylidene **85** was by far the most active complex. The original Crabtree catalyst (Ir(COD)(py)(PCy_3)PF_6) **80**, as well as the NHC complexes bearing ligands **84, 86, 87** took on average 9 hours or longer to reduce cyclohexanone to the corresponding alcohol with TOF's between 8-75, but the cyclohexyl substituted imidazolidine ligated complex quantitatively reduced the same substrate in 10 minutes with a TOF of 2,400.[212] The authors attribute this greater

activity to the fact that the cyclohexyl rings impart less steric constraints on the carbene centre, and contribute a greater degree of electron density onto the metal centre when compared to ligands with aryl wing tips.

2.2.1 Transition metal complexes bearing NHC ligands in transfer hydrogenation

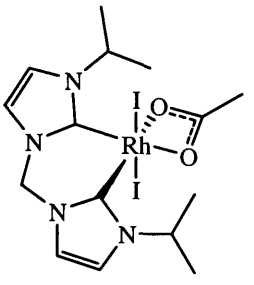
By way of contrast, there are very few examples of high activity NHC pincer complexes for transfer hydrogenation.[213] As anticipated ruthenium and iridium species predominate, and ruthenium complexes generally have lower TON/TOF's relative to their iridium counterparts.[214] During the course of our own studies, Crabtree produced a complex **88** capable of reducing cyclohexanone with a TOF of 6300 h^{-1}, TON of 126,000 and this is currently the gold standard. The reaction took 20 hours at reflux (83 °C), but was accomplished using only 0.0007mol% catalyst.[214b]



88

Figure 30

Rhodium pincer carbene complexes have also been shown to be successful at transfer hydrogenation. **88** demonstrated much faster reduction of aryl substituted ketones



89

Figure 31

(benzophenone: TON 10589, TOF 441) compared to aliphatic ketones (cyclohexanone: TON 1322, TOF 55).[215] This is the opposite trend to that observed for **89**, which is a more efficient catalyst for the reduction of aliphatic ketones (cyclohexanone: TON 19,000, TOF 1,900) than it is for aryl ketones (benzophenone: TON 890, TOF 7).[216]

2.3 Oxidation

The problems involving the facile, high yielding oxidation of alcohols, especially primary ones as discussed in the previous section have been confronted using a myriad of orthogonal methods.[217] Acidic and basic chromium based reagents,[218] Swern type approaches,[219] enzymes,[220] catalytic oxidants[221] and hypervalent iodine reagents such as the Dess-Martin periodinane[222] are among the more commonly used. From the metals that have potential for use in selective oxidations, ruthenium takes a special position owing to its versatility. It is capable of catalysing numerous oxidative transformations such as the oxidation of alkanes, the cleavage of double bonds, the asymmetric epoxidation of alkenes, the oxidation of alcohols and ethers and the oxidation of amines and amides, even the oxidation of H_2O to O_2![223] In the field of alcohol, ether and amide oxidation, ruthenium-based catalysts represent the state of the art and show great potential for application in the fine chemicals industry. Ruthenium is an ideal choice for a metal oxidant since it possess the widest range of oxidation states of any atom, from -2 in $Ru(CO)_4^{2-}$ to octavalent in RuO_4, as well as the most coordination geometries of any element.[224] This is a consequence of, a $4d^75s^1$ electron configuration, with the more common oxidation states of +8 to +3 corresponding to a d^0 to d^5 configuration. Altering the oxidation state and varying the ligands gives a versatile metal centre with the potential to fine tune the oxidative properties of the complex as required.[225] Transition metal-catalysed oxidations have recently attracted considerable interest and a number of oxidants and transition metals have been explored in order to develop methods for mild and selective oxidation of alcohols. Success using ruthenium catalysts[226] has been achieved with N-methyl morpholine oxide,[226a] benzoquinone,[226d] molecular oxygen,[226c,d] iodosylbenzene,[226b] with *tert*-butyl hydroperoxide,[227] chloramine-T,[228] and $NaIO_4$[229] as stoichiometric oxidants.

Ruthenium catalysed oxidation can be divided into two differing mechanistic groups. In the first case, a low valent ruthenium (II) species reacts with an alcohol to form a ruthenium alkoxide **90**, which then, through a process of β-hydride elimination, yields a carbonyl compound and a ruthenium hydride **91**. This hydride is then converted back to the active catalyst either by reaction with a hydrogen acceptor, reacting with an oxidant or producing molecular hydrogen, Figure 32.

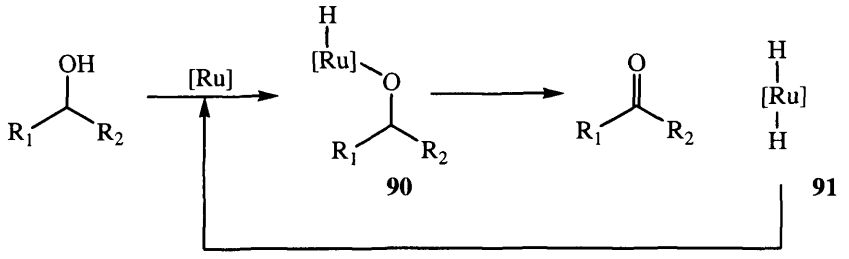


Figure 32

The second mode by which ruthenium oxidation operates is reaction of an alcohol with a high valent (IV, VI, VII) ruthenium-oxo species to form an alkoxy-ruthenium hydroxide complex **92** in a mechanism which is identical to that of Cr-based oxidation. Decomposition of this intermediate ruthenate ester gives the ketone and a molecule of water, with the reduced ruthenium species then being re-oxidised by a stoichiometric oxidant such as an N-oxide (Figure 33).[230]

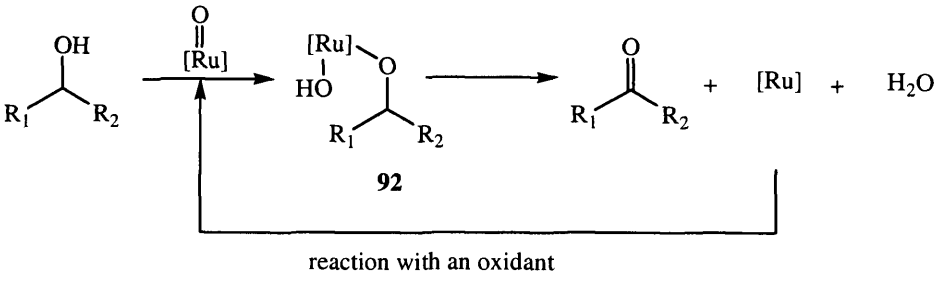
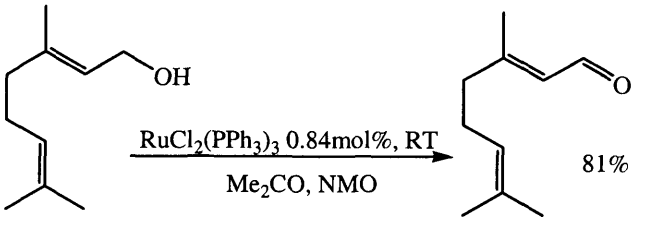


Figure 33

An alternative way to view oxidation is as a dehydrogenation reaction. Similar to transfer hydrogenation, this involves the removal of H_2 from the target molecule but unlike transfer hydrogenation, there is no acceptor molecule, with H_2 being released from the system as a gas. This type of methodology has been successfully applied using Ru NHC[231] and pincer[232] complexes, and was demonstrated as being an efficient method of oxidation, as the reaction is thermodynamically driven, with irreversible loss of H_2.

Application of transition metal catalysis to the Oppenauer oxidation brings about similar improvements as when the same complexes were applied to MPV reductions, with truly catalytic reactions, increased rates and less forcing conditions all becoming achievable. However even with more active catalysts, primary alcohols are still difficult to oxidise by ruthenium catalysis under hydrogen transfer conditions, probably owing to the formation of inactive ruthenium hydridocarbonyl or carbonyl complexes.[233] It is well established that basic conditions accelerate the reaction of ruthenium chloride-tertiary phosphine complexes with primary alcohols resulting in the formation of stable hydridocarbonyl or carbonyl complexes of ruthenium.

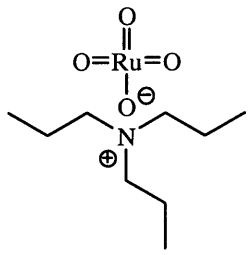
One of the earliest successful examples of ruthenium complexes being applied to catalytic oxidation under mild conditions was published by Sharpless,[226a] who compared several ruthenium sources for the oxidation of alcohols in acetone. By combining the ruthenium source with stoichiometric N-methylmorpholine oxide[234] (NMO), the reaction becomes catalytic with respect to the metal. $RuCl_3.xH_2O$, $Ru_3(CO)_{12}$, and $RuCl_2(PPh_3)_3$ were found to be among the best catalysts he studied, however, on account of cost and solubility, $RuCl_2(PPh_3)_3$, was selected as the lead catalyst. This paper postulates that oxidation proceeds *via* initial attack of the substrate alcohol on the ruthenium centre leading to a Ru-alkoxide. Through the process of β-elimination, a new carbonyl compound is created as well as a ruthenium hydride, which is itself a pre-catalyst. The ruthenium-hydride is then oxidised by NMO to form a ruthenium-oxo species capable of repeating the cycle. We shall return to this proposal in chapter 5 of the present thesis. This particular catalytic system showed an unusual preference for primary alcohols, for example l-decanol being oxidised three times faster than 2-dodecanol. A typical example from the paper is the oxidation of the allylic, primary alcohol, geraniol **93** to citral **94**, Scheme 34.



93 **94**

Scheme 34

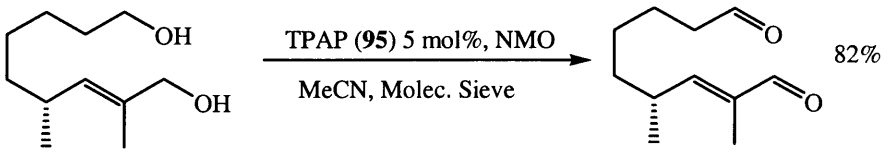
In 1987 Ley and Griffith[235] introduced tetra-*n*-propylammonium per-ruthenate (TPAP) **95** and its tetra-*n*-butyl analogue, TBAB.[236] These ruthenium salts are soluble, non-volatile, air stable, easily prepared oxidants.[237] TPAP and TBAB are less powerful, but all together more selective [Ru (VII) O_4]$^-$ oxidants, than RuO_4 and consequentially, of much greater use in chemoselective organic synthesis.



95

Figure 34

TPAP has gained widespread use in synthesis and is now routinely used for oxidation of primary (Scheme 35) and secondary alcohols, allylic and benzylic hydroxyl groups, lactol and heteroatom oxidation.[238] It is very active in the oxidation of primary alcohols, reactions usually being complete in less than 1 hour using 5 mol% of catalyst, with yields much higher than those seen when using alternative methods.



Scheme 35

In fact, TPAP is so active in the oxidation of alcohols that the oxidation of dodecan-1-ol proceeds smoothly under an atmosphere of air, with no other oxidant, in the temperature range of 65–110 °C, reaching ~70% dodecanal after 2–3 h. At higher conversions, a small amount of dodecanoic acid (less than 5%) is observed.[239]

Progress in the field of oxidation is now focusing on the treatment of by-products generated from the oxidative procedure, or the recycling of co-products. Innovations based on aerobic oxidation or use of innocuous oxidants such as hydrogen peroxide are

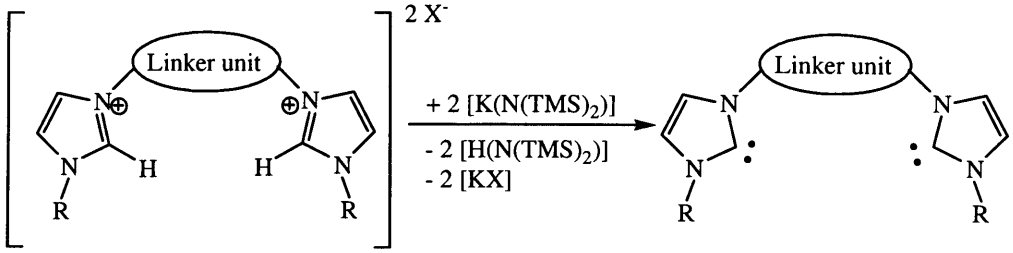
actively sought with the ultimate aim of developing more environmentally friendly chemistry, with a greater degree of atom economy, and it is with this in mind that we started our own oxidation programme which is presented in Chapter 5.

Chapter 3

Ligand and complex synthesis

3.1 Pincer carbenes

As we have seen pincer carbenes by definition, require the use of linkers between the imidazole rings, thereby presenting further potential sites for modification of the ligand to incorporate extra functionality or chirality within the ligand (Scheme 36). However, the linker can also present potential complications in that some sites may be deprotonated by the relatively strong bases sometimes used to form the carbene from the precursor imidazolium salt.[240] Bases such as $K[N(TMS)_2]$, KH, KO^tBu or LDA were therefore introduced to resolve this problem, forming the carbene, whilst not affecting the methylene (or other hydrocarbon based bridge).[241] Care has therefore to be taken with the choice of base used, because certain hydrides yield imidazolidines (addition of hydride) rather than carbene formation.[242] In consequence liquid ammonia or THF have become the preferred solvents for generating the carbene.[243]

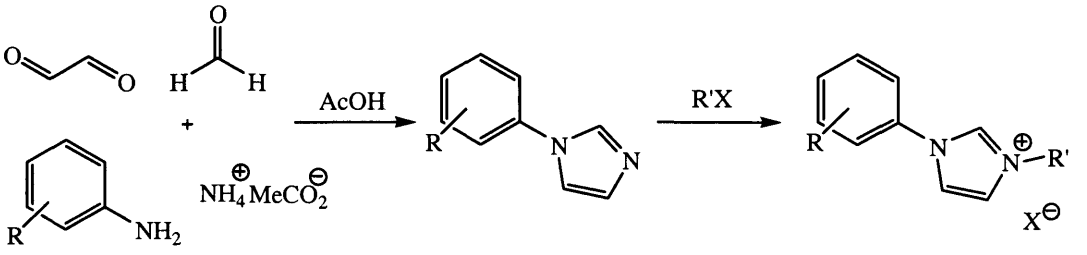


Scheme 36

3.2 Synthesis of pincer based imidazolium salts.

The most frequently used method to access nucleophilic carbenes involve their corresponding imidazolium salts.[244] Although a number of different types of stable carbenes have been isolated, including 1,2,4-triazole-3-ylidenes,[245] thiazol-2-ylidenes,[246] imidazolin-2-ylidines,[247] and benzimidazol-2-ylidenes,[248] imidazole-2-ylidenes[249] are by far the most common. This is due to their increased stability, their capacity for steric and electronic functionalisation, as well as the relative ease of synthesis.

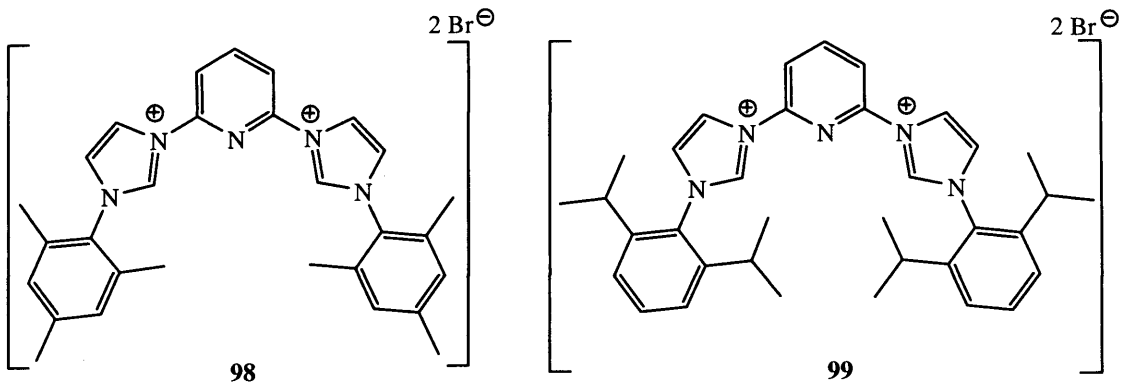
In our studies the aryl-substituted imidazoles used were all synthesised *via* a multicomponent reaction of glyoxal, formaldehyde, a primary aniline, and ammonium carbonate.[250] Subsequent alkylation of these substituted imidazoles yielded the imidazolium salts, Scheme 37.



R= 2,4,6-trimethylphenyl- **96**
R= 2,6-di*iso*propylphenyl-**97**

Scheme 37

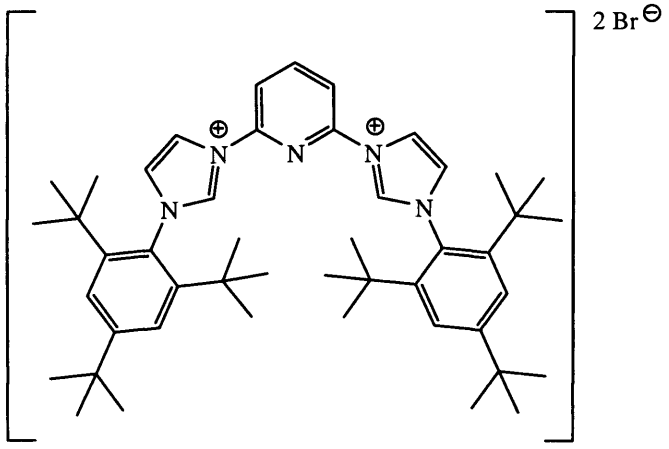
The mesityl substituted pincer **98** and the 2,6-di*iso*propylphenyl based pincer **99** were both synthesised in this manner, with the final quaternisation occurring under solvent free conditions with 2,6-dibromopyridine in a sealed tube. Attempts to perform this quaternisation in refluxing ethanol, acetonitrile or xylene failed, even with prolonged reaction times.



98 **99**

Figure 35

These two ligands were developed in order to mimic analogous phosphine and amine pincers reported by Osborn,[251] and van Koten,[252] which exhibit rich and diverse chemistry. Having the 2,6 trisubstituted pattern on the aryl 'wingtip' results in it being turned on its edge, offering a steric effect in the plane of the carbene similar to that of a methyl group in the case of **98**, or an *iso*-propyl group in the case of **99**. These choices of wingtip were made on the base of a logical progression in steric bulk. Synthesis of the 'super-mesityl' (Mes*, 1,3,5-*tert*-butylphenyl) substituted imidazolium salt **100** was also pursued in order to complete this progressive increase of bulk, Figure 36.

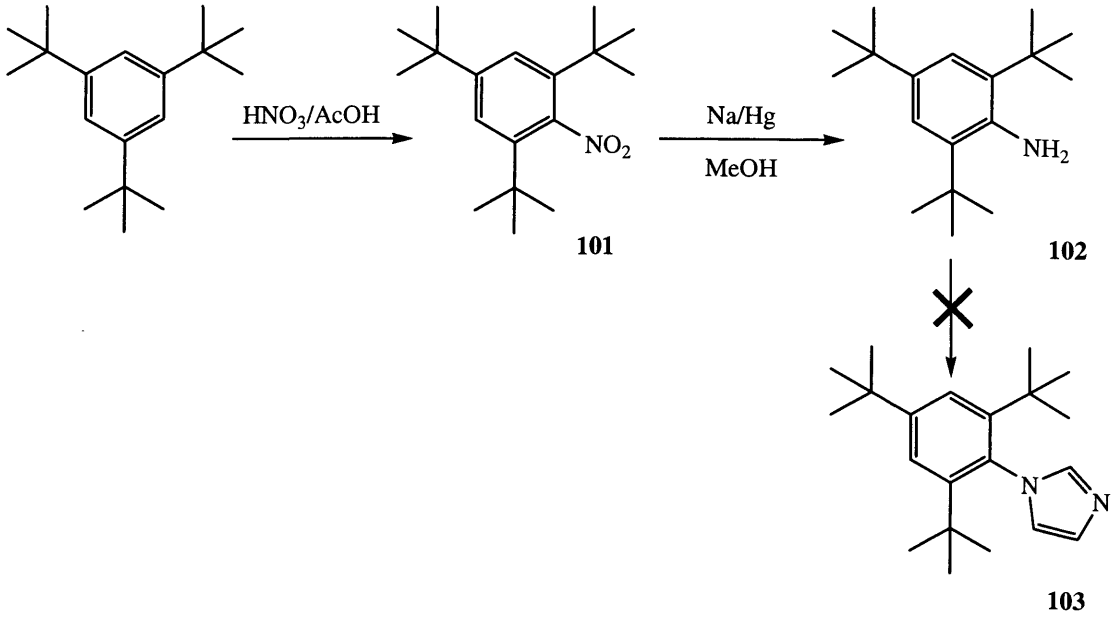


100

Figure 36

Synthesis of the required aniline **102** to produce the super-mesityl ligand was achieved *via* a simple nitration-reduction protocol of the commercially available trisubstituted benzene. Attempts to form imidazole **103** from 2,4,6-tri-*tert*-butylaniline using the

multicomponent methodology that was successful for **98** and **99** was hampered by the insolubility of the aniline in the reaction solution. We overcame this issue by adding ethanol to the reaction solution (50%, v/v), but the reaction still failed even with extended reaction times.

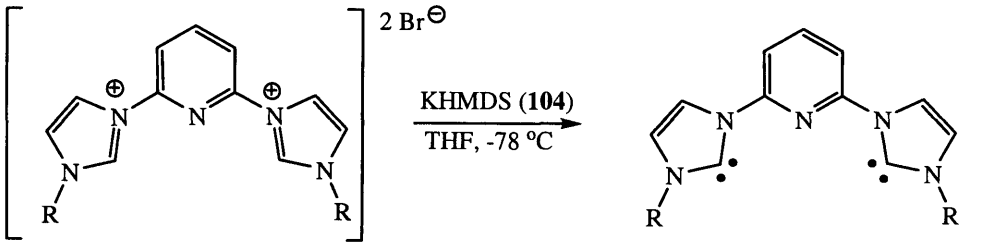


Scheme 38

3.2.1 Pincer complex generation

3.2.1.1 Pincer complex generation *via* the free diaminocarbene

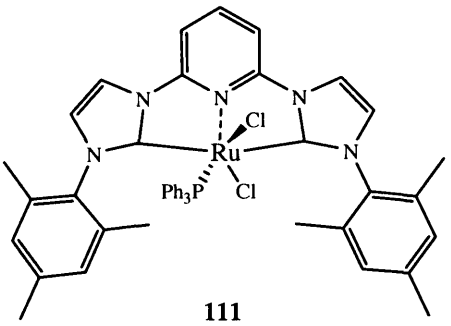
Following literature precedent,[253] both **98** and **99** were deprotonated using KHMDS **104** in THF, and the corresponding free carbenes, **105** and **106**, were isolated, Scheme 39.



Scheme 39

$RuCl_2(PPh_3)_3$ **107**, $RuHCl(PPh_3)_3$ **108**, $RuHOAc(PPh_3)_3$ **109**, and $RuCl_2(nbd)(Py)_2$ **110** were all prepared following procedures described in the experimental section (Chapter 9). These Ru (II) sources were selected as suitable precursors to combine with the preformed carbenes, as the existing ligands could be easily displaced by the carbene ligands of the pincer.

We carried out a degree of optimisation work on the combination of the $RuCl_2(PPh_3)_3$ **107** and the isolated carbene **105**, to form the complex **111**. Addition of a suspension of **107** in THF, to a solution of the carbene in THF, both at -78°C, followed by warming to -20°C over a period of 12 hours resulted in a 28% yield.



111

Figure 37

This yield was improved to 34% by reversing the order of addition. Presumably when the carbene is added to the metal, it rapidly comes in contact with a metal atom, and forms the pincer complex due to the increased stability of forming the bis-chelated conformation. The reverse of this situation is when the metal is added to the carbene. As there is an excess of carbene, the metal can chelate to one carbene, but, before it can close around to form the pincer complex, it may be intercepted by a second carbene molecule to give the structure depicted in Figure 38. It is conceivable that the formation of complex metal carbene dimers/oligomers could occur, although we do not have any experimental evidence for this.

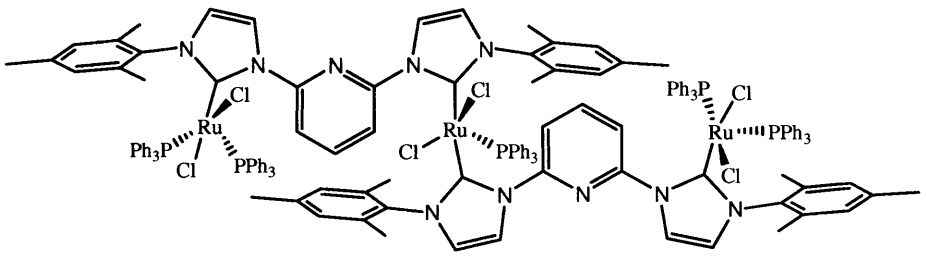
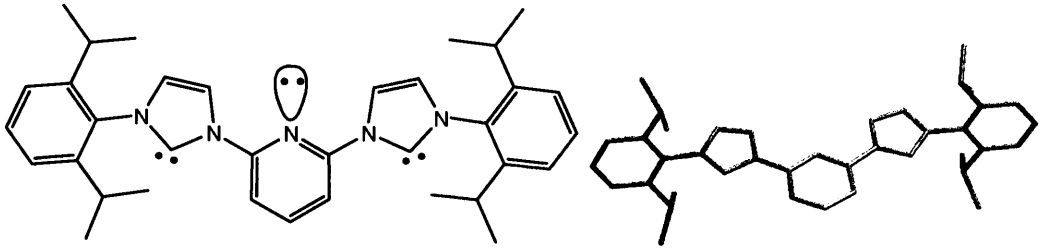


Figure 38

Danopoulos determined the structure of the free carbene **106** by diffraction methods. The molecule is strictly planar adopting a conformation in which the carbene and the pyridine lone pairs are mutually *anti*, possibly in order to minimise lone pair repulsions. **106** is the first example of a structurally characterized dicarbene.[254]

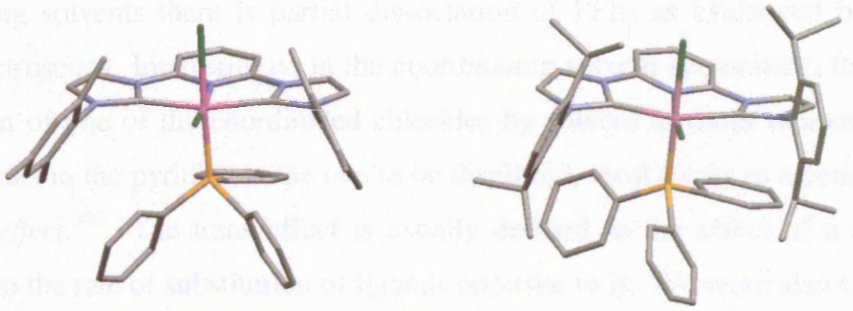


106

Figure 39

This may indicate that the rate-limiting step of the complex formation is the conformational 'flip' required to take the pincer from its *anti* confirmation to the *syn* conformer, which is required in order for the *bis*-chelate to form. This could also explain the difference in the yield of complex depending on order of addition. The effect of combining both compounds in their solid state at –78 °C and adding THF, also at -78°C was studied. This offered a similar yield to the initial method (26%). The final improvement was post addition of the carbene to the metal, the reaction solution is allowed to warm to room temperature over 3 hours, followed by a 4 hour room temperature stir. We believed that the additional thermal energy in the system might encourage the *anti-syn* isomerisation. Indeed, this resulted in a 45% isolated yield of complex, and this method was then followed for all future pincer complex syntheses.

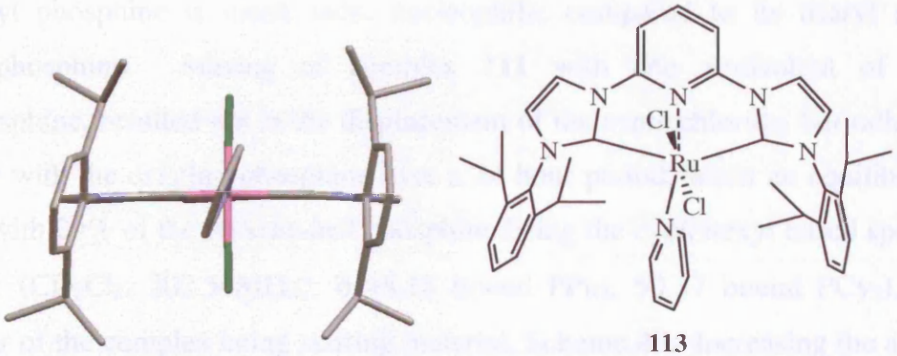
Combination of **105** or **106** with $RuCl_2(PPh_3)_3$ **107** resulted in the isolation of **111** or **112** respectively. These two orange microcrystalline ruthenium complexes gave the X-Ray structures presented in Figure 40.



111 **112**

Figure 40

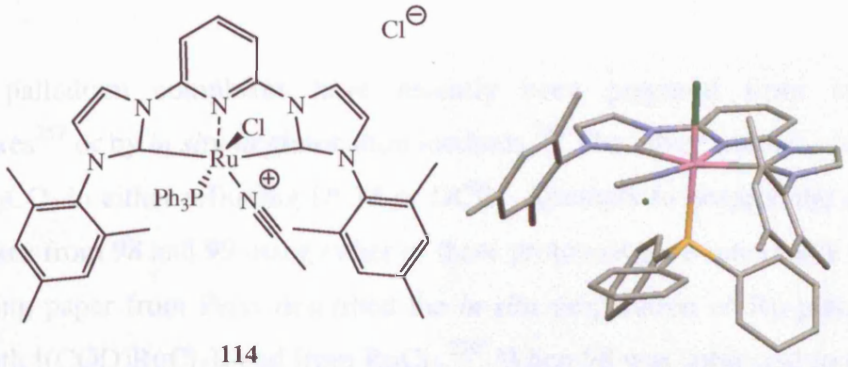
Complexation of **105** and **106** with the metal precursors $RuHCl(PPh_3)_3$ **108**, $RuHOAc(PPh_3)_3$ **109**, produced complex mixtures of products. In the case of $RuHCl(PPh_3)_3$ **108**, a green material was produced, with loss of the hydride signal whilst with the acetate complex **109**, rapid darkening of the reaction solution occurred with disappearance of the NMR signals corresponding to the starting ruthenium species. Combination of **106** with **110** with pyridine functionalised ruthenium source **110** produced a complex **113** in which the aryl wingtips are able to adopt a perpendicular arrangement to the plane of the carbene, as there is no bulky phosphine ligand to distort their conformation, Figure 41.



113

Figure 41

In all cases, the C-N-C chelate system occupies three meridonal sites and the two chlorides are mutually *cis*. Although ruthenium complexes with monodentate imidazolin-2-ylidenes and imidazol-2-ylidenes had been reported[255] at the time of our synthesis, these were the first examples of a chelating bis carbene. In solution, in non-coordinating solvents there is partial dissociation of PPh_3 as evidenced by 31P{1H} NMR spectroscopy. Interestingly, in the coordinating solvent acetonitrile, there is rapid substitution of one of the coordinated chlorides by solvent at room temperature. The chloride trans to the pyridine is the one to be displaced, most likely as a consequence of the *trans effect*.[256] The trans effect is usually defined as the effect of a coordinated ligand upon the rate of substitution of ligands opposite to it. We were also successful in generating x-ray data for this yellow cationic species **114**, Figure 42.

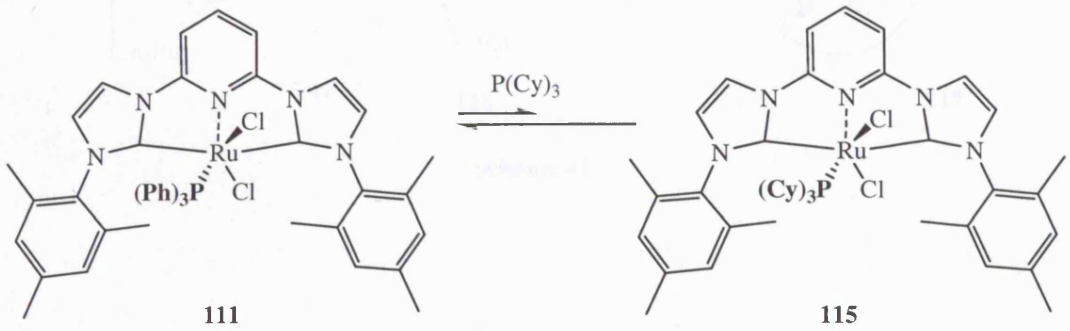


114

Figure 42

With the observed facile removal of the trans chloride ion from the complex we then investigated the reactivity of complex **111** towards another coordinating ligand. Tri-cyclohexyl phosphine is much more nucleophilic compared to its triaryl analogue, triphenylphosphine. Stirring of complex **111** with one equivalent of tricyclo-hexylphosphine, resulted not in the displacement of the *trans* chloride, but rather a slow exchange with the existing phosphine over a 24 hour period, when an equilibrium was reached with 29% of the coordinated phosphine being the cyclohexyl based species **115** (^{31}PNMR (CD_2Cl_2, 202.50MHz): δ 48.18 bound PPh_3, 50.37 bound PCy_3), and the remainder of the complex being starting material, Scheme 40. Increasing the amount of cyclohexyl phosphine did not significantly alter this equilibrium and the compound was never isolated. In retrospect, the considerable bulk of the tricyclohexyl phosphine,

especially in comparison to the linear framework of the acetonitrile, rendered such reactions difficult.

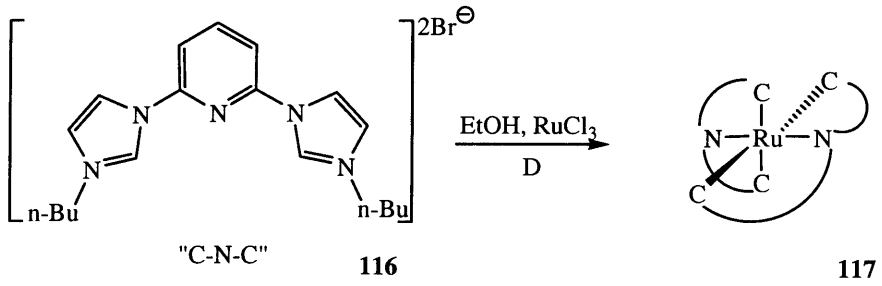


111 115

Scheme 40

3.2.1.1 *In-situ* pincer complex generation from imidazolium salt

Pincer palladium complexes have recently been prepared from silver carbene complexes[257] or by *in situ* deprotonation methods.[258] The silver sources used were Ag_2O and Ag_2CO_3 in either refluxing DCM or DCE. Attempts to prepare the silver carbene complexes from **98** and **99** using either of these protocols gave intractable mixtures. An interesting paper from Peris described the *in-situ* preparation of Ru-pincer complexes from both $[(COD)RuCl_2]_n$ and from $RuCl_3$.[259] When **98** was subjected to the conditions outlined in the paper, a brown solid was isolated, which was demonstrated by ^1H NMR to be a mixture of several unidentified products. Dissolution of this solid in DCM resulted in a red solution, which when columned, gave a red fraction, that within seconds turned green. Attempts to do an anhydrous/inert atmosphere column on the crude brown material resulted in similar results. The NMR of the green material was not indicative of either the expected product or starting material. This methodology was not pursued any further since, according to the paper by Crabtree, the product produced when the imidazolium 'wingtips' were alkyl rather than aromatic as in **98**, was a catalytically inactive complex containing two pincer systems around a single metal centre **117**.



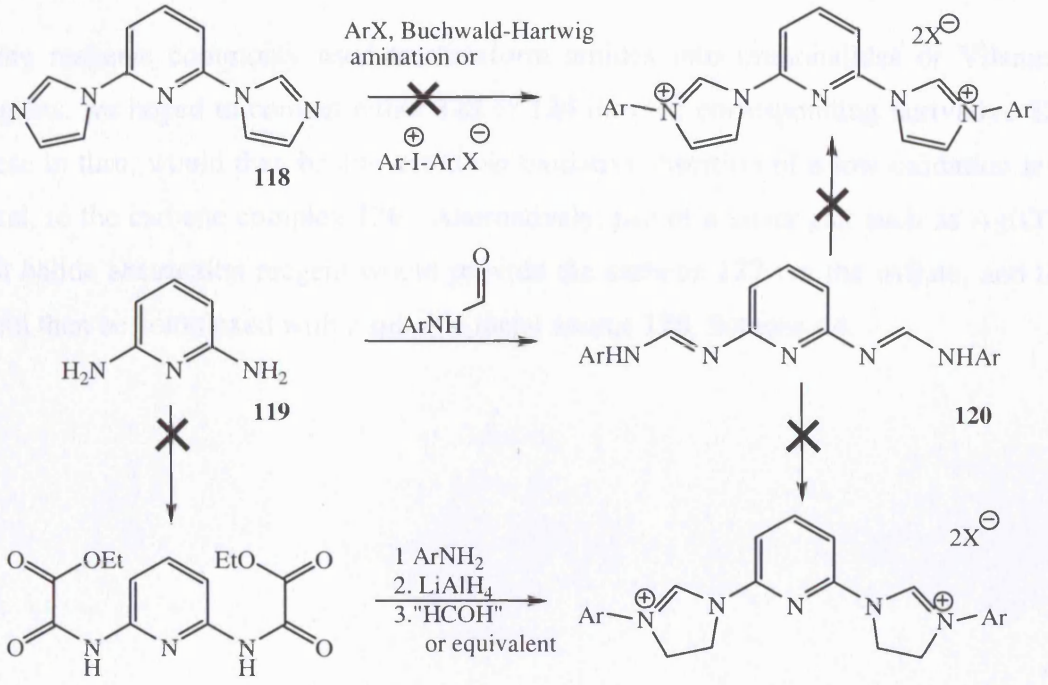
"C-N-C" **116** **117**

Scheme 41

3.3 Novel Methodology toward ligand and complex synthesis

3.3.1 Imidazolium precursors

Many routes were explored for the synthesis of the basic pincer scaffold, some of which are summarised in a general manner in Scheme 42. All routes were either low yielding or failed in the final stage to cyclise to the *bis*-imidazolium salt. At the time of writing the most recent method for the synthesis of asymmetric dihydro-imidazoles yields the simple product in only 27% after a 4 step route, demonstrating the need for high yielding practical synthesis of this type of compound.[260]

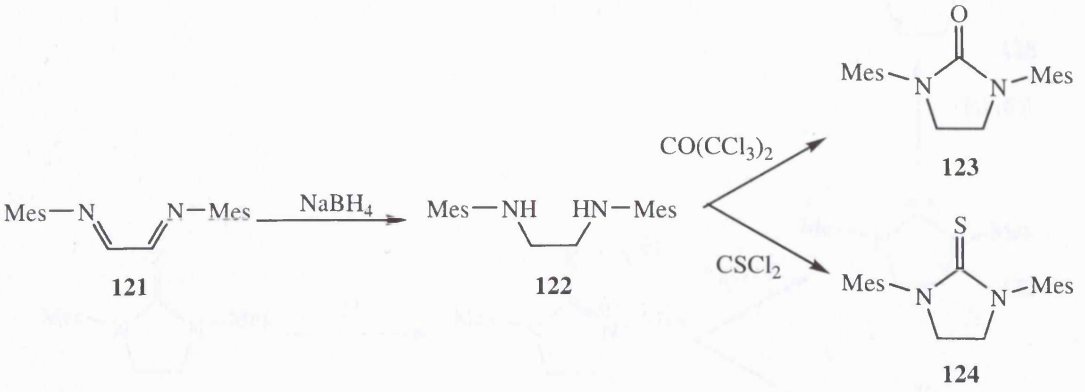


Scheme 42

3.3.2 Iminohalides and ureas

A novel approach that we pursued at this time for direct carbene complex formation was based on the anticipated conversion of a urea, in a single step, to a carbene complex.[261] The synthesis of a urea, is of course, simpler than that of an imidazolium salt. Reduction of the readily accessible 1,2-*bis*-mesityl-diazabutadiene **121** provided the

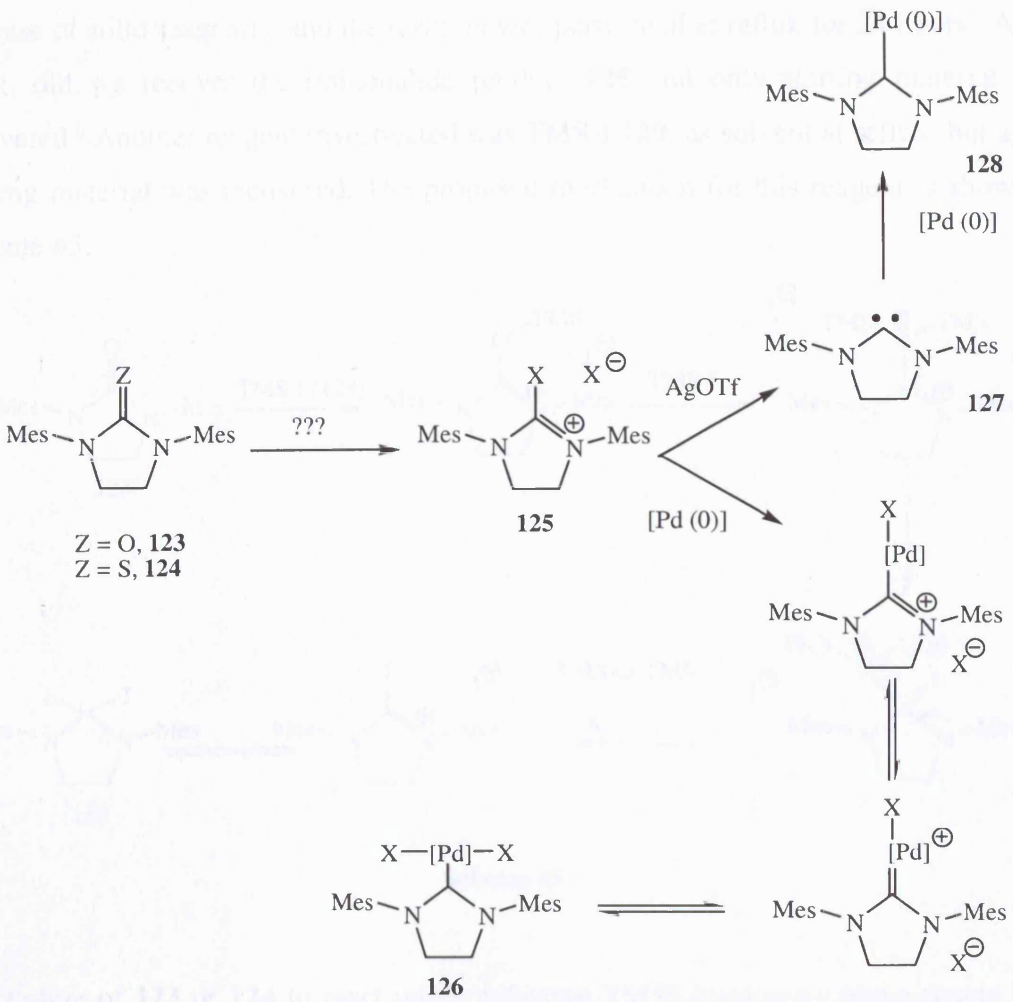
corresponding 1,2 diamine **122**, which was cyclised to either the urea **123** or thiourea **124** derivatives (Scheme 43).



121 **122** **123** **124**

Scheme 43

Using reagents commonly used to transform amides into iminohalides or Vilsmeier reagents, we hoped to convert either **123** or **124** into the corresponding derivative **125**. These in turn, would then be converted *via* oxidative insertion of a low oxidation level metal, to the carbene complex **126**. Alternatively, use of a silver salt such as Ag(OTf) as a halide abstraction reagent would provide the carbene **127** *via* the triflate, and this could then be complexed with a suitable metal source **128**, Scheme 44.



Scheme 44

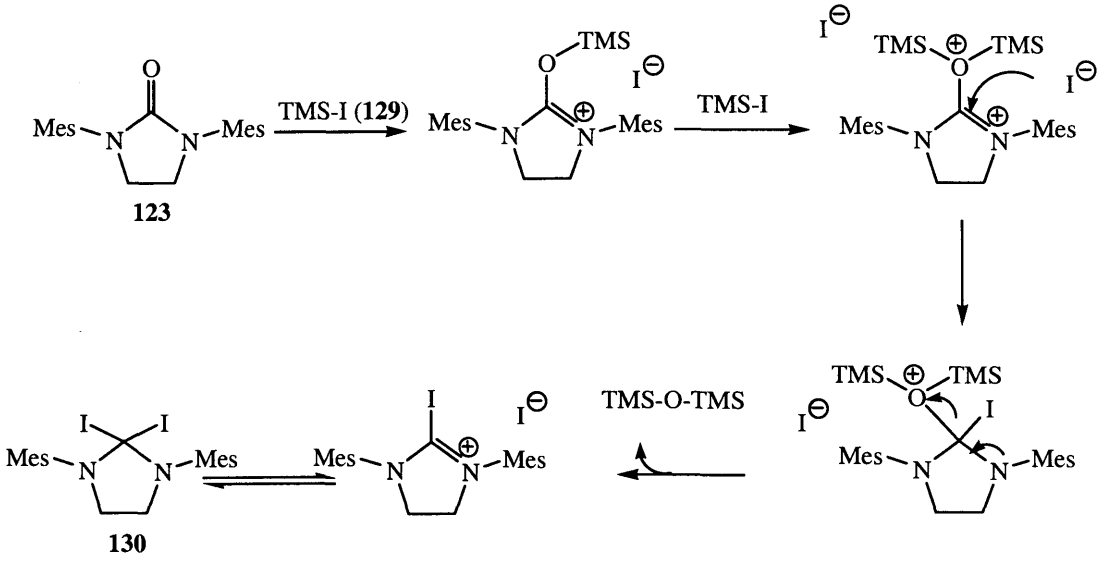
We investigated a range of reagents for the first step of this reaction sequence, as summarised in Table 2.[262]

$(CO)_2Cl_2$	PCl_5	PPh_3 / CCl_4
$(CO)_2Br_2$	PBr_5	$CO(CCl_3)_2$
$POCl_3$	$PCl_5/POCl_3$ (solvent)[263]	$CO(CCl_3)_2$ / NaI
PCl_3	PPh_3 / I_2	$COCl_2$

Table 2

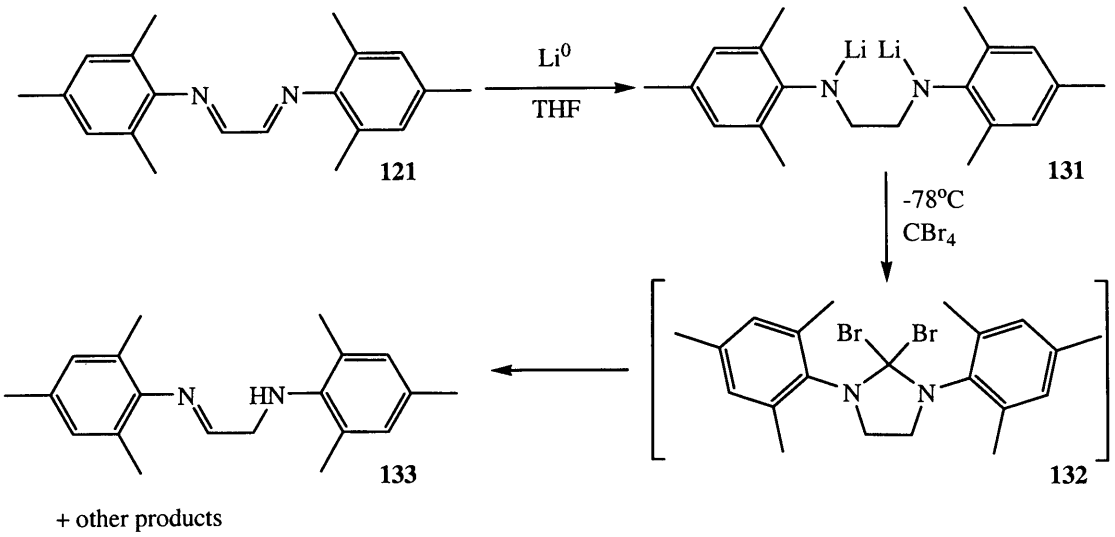
For each reagent, 1 molar equivalent was initially reacted with either the urea **123** or the thiourea **124**. When this was not successful, the number of equivalents was increased to the point where the reagent acted as solvent (or 100 equivalents in a suitable solvent in

the case of solid reagents), and the reaction was performed at reflux for 24 hours. At no point, did we recover the iminohalide product **125** and only starting material was recovered. Another reagent investigated was TMS-I **129**, as solvent at reflux, but again starting material was recovered. The proposed mechanism for this reagent is shown in Scheme 45.



Scheme 45

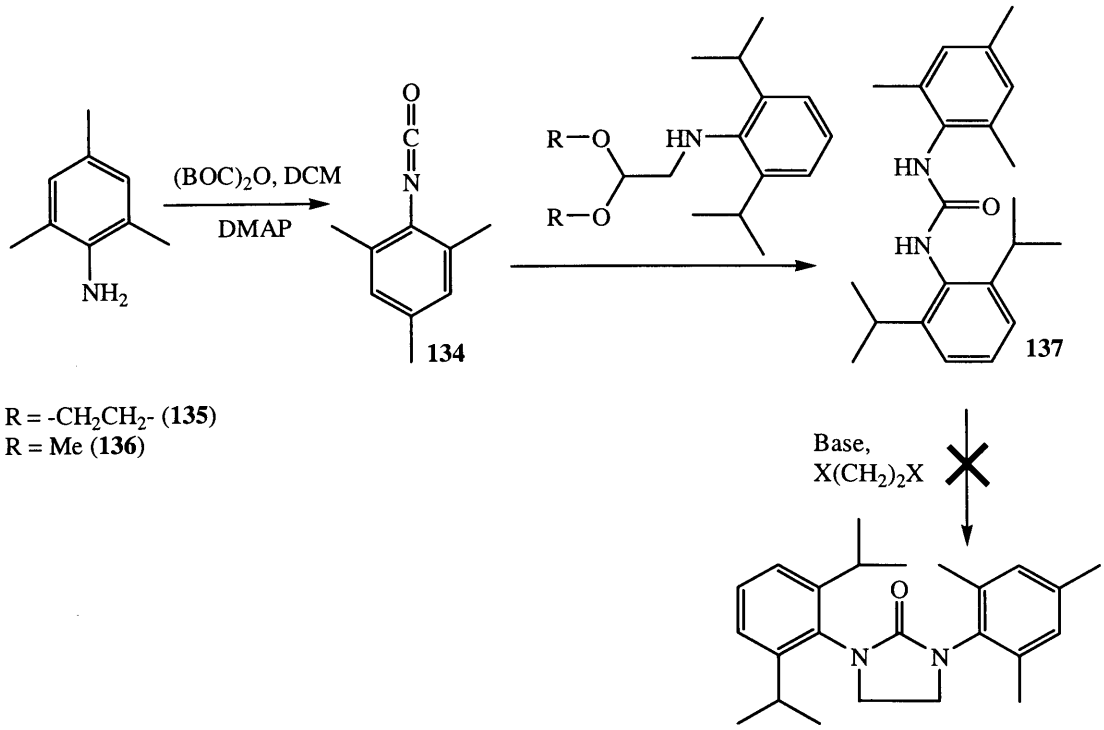
The failure of **123** or **124** to react under refluxing TMSI conditions demonstrates how electron deficient the *bis*-aryl urea is. We had expected it to react as an amide would under typical Vilsmeier Haack type conditions.[264] It was only when we combined freshly prepared TMSI **129** with the very strong oxophilic Lewis acid TMSOTf (5%),[265] that we saw conversion to the iminium iodide (14%) **130** after 12 hours reflux. Due to the forcing conditions required however we felt that the original aim of finding a facile route to the carbene complex had been compromised, and this approach was not pursued any further, other than briefly exploring the ring closure of the 1,2-diaza species **121** as outlined in Scheme 46.



Scheme 46

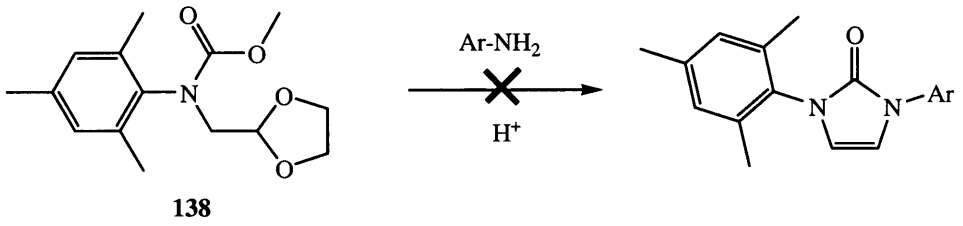
Thus, single electron reduction of diazabutadiene **121** and reaction with CBr_4 produced a compound with an NMR which was indicative of the expected product **132**. Any attempted isolation of this material however led only to recovery of the fully reduced **122** and partially reduced **133** starting materials.

At this time methods were also developed to make unsymmetrical cyclic ureas in anticipation of the iminohalide method being successful. The most flexible method found was *via* an intermediate aryl-isocyanate **134** formed from the reaction between an aniline and BOC anhydride in the presence of DMAP. Attack on this isocyanate **134** by a preformed aniline acetal **135** or **136** then gave the acyclic, deprotected urea **137**. Attempted cyclisations of **137** using a variety of bases (K_2CO_3, NaH, KH, *n*-BuLi, *t*-BuLi) and solvents (THF, DMF, DMSO, Dioxane, methanol) in conjunction with either 1,2-dibromo- or 1,2-diiodo-ethane was unsuccessful, Scheme 47.



Scheme 47

Attempts to promote an acid mediated ring closure of **138** in the presence of an aniline also failed.

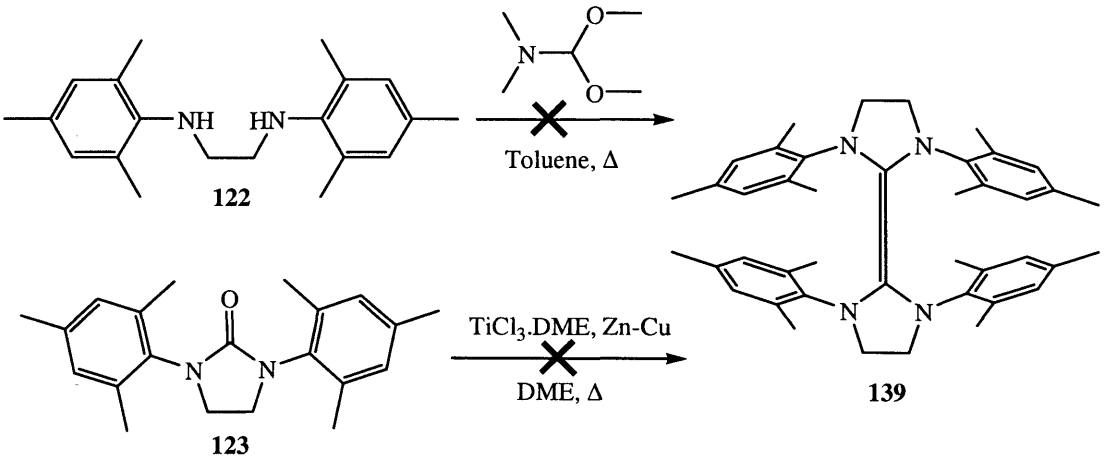


138

Scheme 48

Other potential routes to carbene type precursors which proved to be unsuccessful due to the electron deficient nature of the urea involved McMurray type couplings. It was initially hoped that we could produce electron rich tetraminoalkenes (e.g. **139**) which could undergo reversible cleavage in the presence of a suitable transition metal to yield the corresponding complex. A condensation/dimerisation approach using DMF acetal was the first approach. This is a method used for synthesis of the required alkenes, but is generally described with alkyl substituents on the nitrogen atom, the only example of using this methodology with aromatic substituents was with the very electron rich *p*-

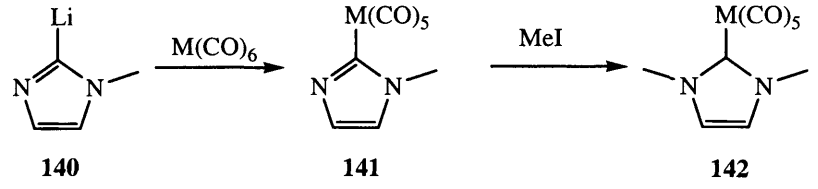
dimethylamino substituted aniline ring.[266] The second attempted approach used the more traditional titanium mediated McMurray conditions,[267] taking advantage of the optimised Zn-Cu couple reductive conditions rather than the more common $LiAlH_4$ method.[268]



Scheme 49

3.3.3 Metallation-quaternisation

An attractive alternative for the formation of the desired NHC metal complexes would involve lithiation of an N_1 substituted imidazole at the most acidic C_1 position. Reaction of this anion e.g. **140** with a suitable metal source, e.g. a metal halide, would result in transmetallation and elimination of an equivalent of lithium salt. Subsequent quaternisation of this organometallic species would then give the carbene complex e.g. **142**, without ever forming or isolating an intermediate carbene thus minimising the possibility of complex degradation. There is a limited number of examples in the literature where this approach has been explored.[269] An example of this methodology is presented in Scheme 50.[269b]

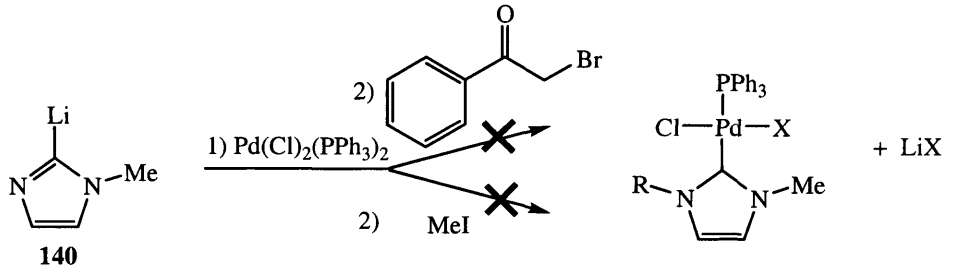


140 **141** **142**

M = Cr, Mo, W

Scheme 50

In the event however, when the lithium anion of 1-methylimidazole **140** was reacted with $Pd(Cl)_2(PPh_3)_2$ in THF, and subsequent quaternisation attempted using either methyl iodide or bromoacetophenone, only a mixture of starting material and the corresponding imidazolium salt was recovered, with no evidence for carbene complex formation (Scheme 51).

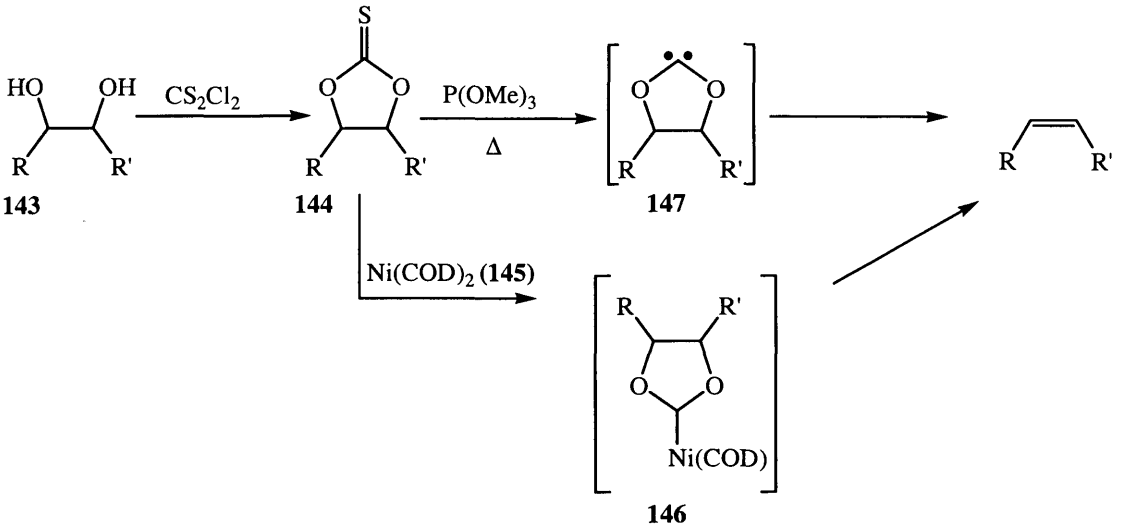


140

R = Me, $PhCOCH_2$

Scheme 51

The Corey Winter olefination involves conversion of a 1,2-diol e.g. **143** into an alkene *via* a thionocarbonate intermediate **144**, Scheme 52.[270] The reaction can be considered to proceed through the formation of a carbene, before spontaneous loss of CO_2. The reaction generally uses very forcing conditions, but substituting the traditional phosphite for $Ni(COD)_2$ **145** in the reaction mixture, results in a very fast, facile reaction producing the desired alkene.[271]



Scheme 52

We believed that if this methodology could be transferred to thioureas (e.g. **124**) the free carbene or a nickel complex thereof could be formed. The Corey Winter reaction gives an alkene as the final product since CO_2 is rapidly and irreversibly lost from the substrate due to the instability of the intermediate dialkoxycarbene **147** (or **146**) under the conditions of the reaction. We were anticipating that the diamino-analogue would be stable under the reaction conditions, and hence allow for its isolation or further reaction. There may also be the possibility of *in-situ* complexation to other transition metal sources should they be present in the reaction mixture. Early indications for this methodology look promising. Treatment of frozen, freshly prepared $Ni(COD)_2$ **145** in DMF at –78 °C with 1,3-dimethylimidazolidine-2-thione **124** and subsequent gradual warming to room temperature over 1 hour, followed by a further 2 hour stir at room temperature led, after workup, to a compound presenting NMR data which were consistent with formation of a Ni-COD-carbene complex. Further work on this approach may prove to be beneficial.

Chapter 4

Transfer Hydrogenation

4.1 Background

With a number of novel NHC transition metal complexes now in hand, our attention turned to their potential use as catalysts. In the first instance, we were naturally attracted to the use of ruthenium complexes as potential transfer hydrogenation catalysts. As already discussed in the introductory overview, such reactions offer many potential advantages, especially for the product development processes in the fine chemicals and pharma-industries.

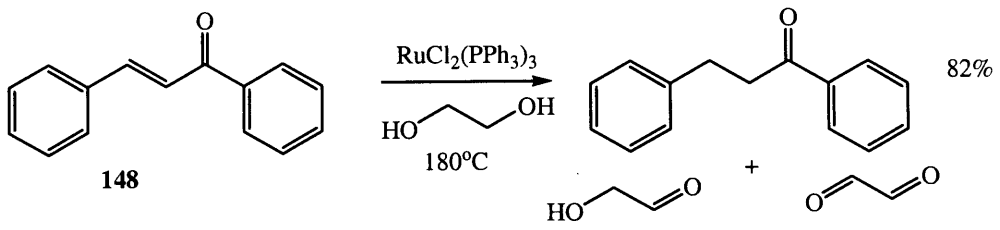
4.2 Development of methodology for transfer hydrogenation using pincer complexes

Catalyst Stability and operating protocol.

Due to the relatively small amounts of catalyst required during our investigations (generally between 2-4 mg per reaction) it proved to be more expedient to use a prepared standard solution of the catalyst, which could then be accurately transferred to the reaction vessel. The transferred aliquot was then concentrated *in situ* to return the solid catalyst. A solution (1 mg / mL) of each complex was prepared in DCM (anhydrous) and stored under ambient conditions in a stoppered volumetric flask. Over a period of 7 days its catalytic activity was monitored along with its NMR profile. There was no significant change in either of these stability criteria over the test period. We therefore consider that there are no adverse problems associated with keeping solutions of **111** or **112** on the bench for up to one week, without recourse to the use of meticulous anhydrous/anaerobic techniques during daily use.

4.2.1 Initial studies

Our initial thoughts centred around the idea that some clues as to potential operating conditions for transfer hydrogenation using ruthenium NHC pincer complexes as catalysts might be found by comparison with known reactions using $RuCl_2(PPh_3)_3$. This included a report by Sasson and Blum in 1971 that demonstrated transfer hydrogenation of chalchone **148** at 200°C in benzyl alcohol in 2 hours[272] using $RuCl_2(PPh_3)_3$.[273] This method was later improved by use of ethylene glycol as the hydrogen source, achieving similar results in less than 1 hour at 180°C.[274] Maitlis demonstrated that methanol can be used as a hydrogen source, and using the same catalyst as Sasson *et al*, reduced cyclohexanone to cyclohexanol in 5 hours at 150°C.[275]



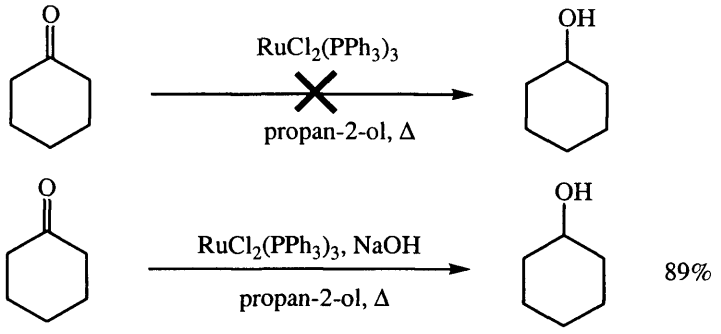
Scheme 53

Transfer hydrogenation depends on several variables such as concentration, temperature and hydrogen donor, and a review on these variables as well as useful insights to the mechanism, was published in 1975.[276] It is likely that the rate-determining step in transfer hydrogenation is the dehydrogenation of the hydrogen donor. Cole-Hamilton discovered that the presence of a base has a dramatic effect on the rate of dehydrogenation. He identified the role of the base as assisting with the generation of a nucleophilic alkoxide anion, which is capable of attacking the ruthenium complex much more rapidly than the protonated alcohol.[277] This paper was specifically studying the dehydrogenation of substrates[278] and not the intramolecular transfer of hydrogen between substrates, however the similarities between the two mechanisms soon led to the findings been applied to transfer hydrogenation.

Our initial experiments therefore used the two pincer complexes **111** and **112** in conjunction with the ethylene glycol based conditions published by Sasson and Blum[274] (*Method A*). We view our pincer complexes as being similar to $RuCl_2(PPh_3)_3$ in which 2 PPh_3 ligands have been replaced by the pincer system, and a further 2 electrons being donated to the ruthenium atom by the pyridine ring that does not occur with the parent compound. Sasson used 20 mol% of $RuCl_2(PPh_3)_3$ to promote the reaction, but for initial experimental work we used 5 mol% catalyst, as the aim was to demonstrate the greater stability of NHC based complexes as opposed to the corresponding phosphine complexes. Chalchone **148** is a standard test substrate for transfer hydrogenation as it contains an α,β-unsaturated group thereby giving useful indications to the chemoselectivity of a system, and hence we attempted its reduction. Unfortunately we failed to reduce any of the test substrate under these conditions. Even after increasing the catalyst loading (20 mol%) and extending the reaction time to 24 hours, no reduced material we detected. It is possible that the pincer catalyst is unable to dehydrogenate ethylene glycol under these conditions (*vide infra*). This results in the absence of the

necessary ruthenium hydride and hence reduction of the substrate is not possible. The chelation of chalchone to the ruthenium species in Sasson's work was marked by the solution turning red. We observed no such colour change when using ruthenium complexes **111** or **112**.

Bäckvall *et al* have published a method for transfer hydrogenation using $RuCl_2(PPh_3)_3$ that takes advantage of base co-catalysis, coupled with the use of propan-2-ol as the hydrogen source.[279] When a solution of cyclohexanone in propan-2-ol is treated with $RuCl_2(PPh_3)_3$ at 82°C, no formation of cyclohexanol is observed. However, the addition



Scheme 54

of sodium hydroxide (2.4 mol%) activates the transfer hydrogenation mechanism, and in one hour an 89% conversion to cyclohexanol was observed (Scheme 54), corresponding to an average 890 turnovers per hour. The initial turnover frequency (TOF) measured during the first 15 minutes is 1800 h^{-1}, which rapidly decreases during the course of the reaction. This reduction in rate is indicative of either catalyst decomposition, or an equilibrium point being reached. As full conversion is observed when the acetone formed during the reaction is distilled from the reaction mixture, it is indicative that the limiting effect had been an equilibrium point.

4.2.2 Propan-2-ol based conditions for aldehydes

We therefore adapted these conditions for our next investigation of the catalytic properties of NHC pincer complexes **111** and **112** (*Method B*). Using tolualdehyde as a convenient simple test substrate, we attempted its reduction. The first successful conditions comprised of a solution of *p*-tolualdehyde in propan-2-ol (2.0 M solution), NaOH (10 mol%), and **111** (0.03 mol%) at reflux for 24 hours, at which point no starting material remained. Along with the product alcohol, a pale yellow material, polymeric in appearance, was present. Analysis of the crude reaction mixture by GC indicated the presence of *p*-tolyl alcohol and a trace of starting aldehyde. Concern however surrounded the fact that the product was expected to be a white crystalline material and our material was a yellow oil. HPLC analysis (internal standard based quantification) was conducted and demonstrated the presence of a significant impurity not seen *via* GC analysis, but accounting for two thirds of the material. The ^{1}H NMR of the crude oil shows the expected peaks for *p*-tolyl alcohol, but with a large amount of 'tailing' around both the aromatic region and the tolyl group, Figure 43. Mass spectrometry demonstrated an approximate Gaussian type distribution of product masses between *m/z* 300-450 amu, and a second significant similar distribution of masses between *m/z* 450-600 amu, that could signify that the yellow material is polymeric. The fact that this material was not detected in our GC analysis gives further credence to the possibility that it may be polymeric in origin. Only 25% of *p*-tolylalcohol was isolated from this set of reaction conditions.

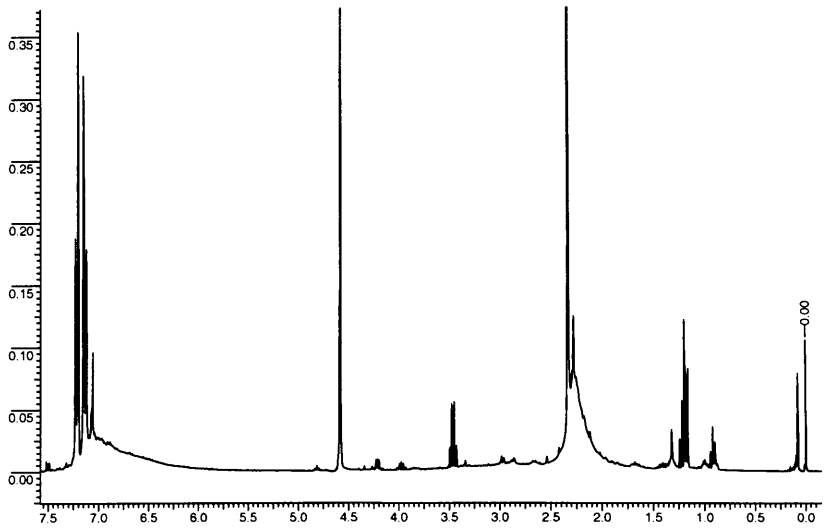
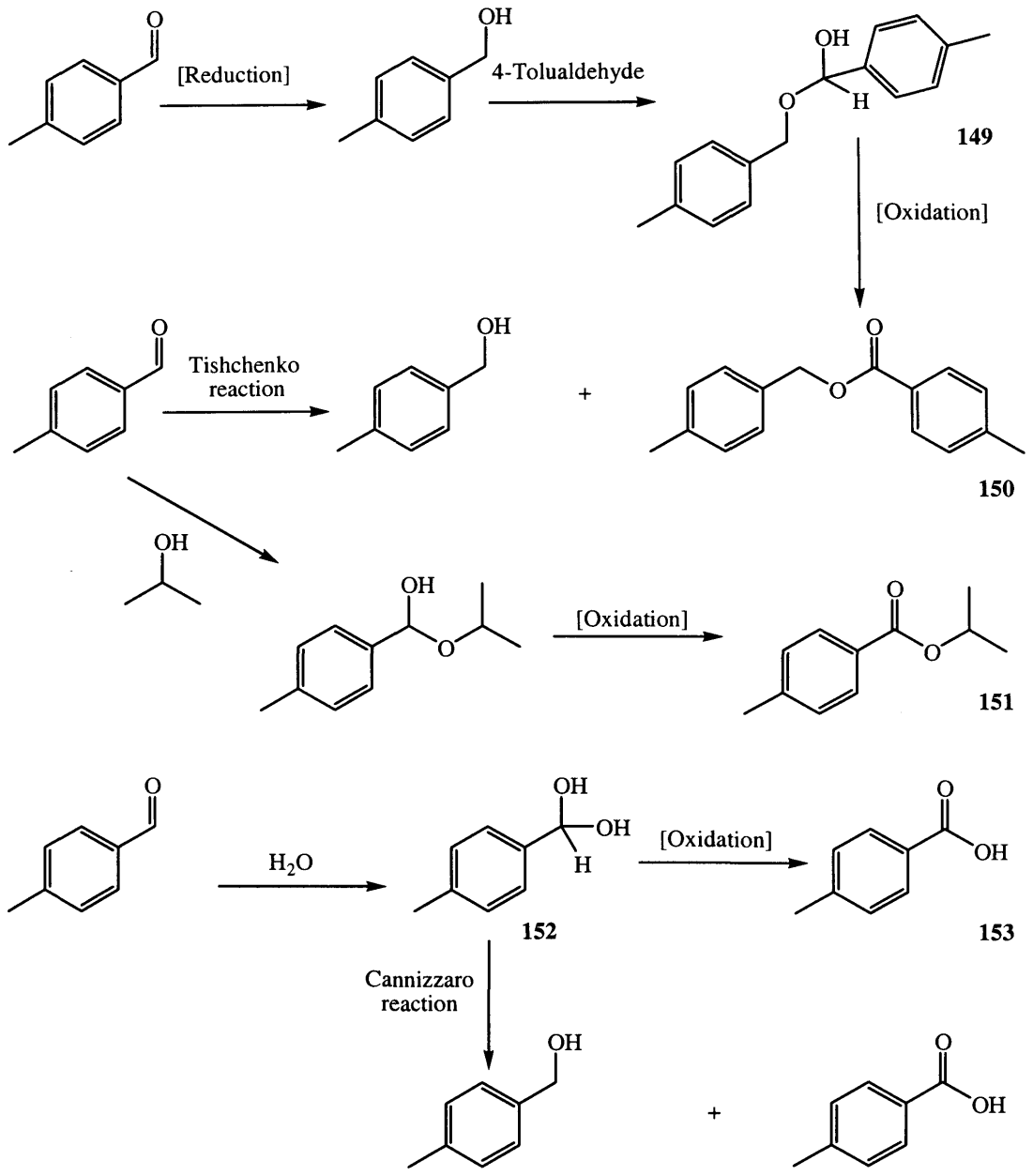


Figure 43

Figure 1

NMR detailing the polymeric nature of the unknown impurity

It was apparent that one or more unidentified side reactions were consuming our starting aldehyde, which, under the basic conditions of the reaction, was not unexpected. Under the basic conditions of the reaction solution, it would be possible for a molecule of product alcohol, to attack a molecule of starting aldehyde. The intermediate hemiacetal **149** thus formed, may be oxidised by the Ru complex to the ester **150**. In a similar fashion, reaction of propan-2-ol with *p*-tolualdehyde would lead to the corresponding *iso*propyl ester **151**. We recorded no analytical evidence for the formation of an ester (except for a weak peak in the Mass spectrometry data of the crude reaction mixture), essentially ruling this possibility out. A further potential side reaction is the Tishchenko[280] reaction, which results in the disproportionation of two molecules of aldehyde to one molecule of ester **150** and one of alcohol, but as already mentioned, we saw no evidence for ester formation. Should water be introduced into the system, the hydrate **152** of the starting aldehyde could theoretically form, which may then be oxidised to the acid **153**. As the reaction was performed under anhydrous conditions however, with all starting materials purified and dried before use, this seemed rather unlikely. Even with 10 mol% of NaOH added, there is insufficient hydroxide to effect the hydration of all the starting material, and so for these reasons, another disproportionation reaction, the Cannizzaro reaction[281] is unlikely to be occurring to a significant extent, Scheme 55.



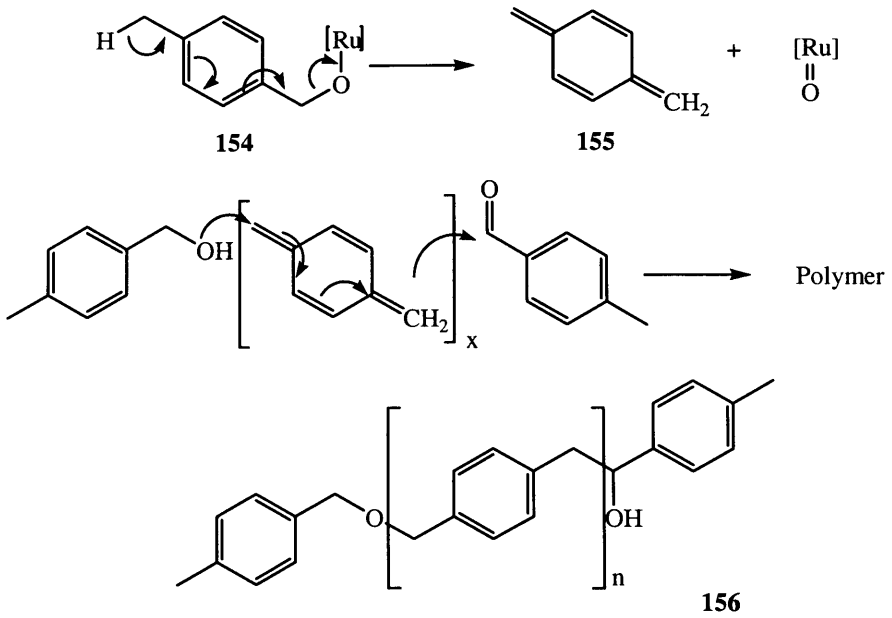
Scheme 55

In an attempt to minimise the unknown side reactions, the reaction was performed again, but under more dilute (0.1 M) conditions.[282] After 24 hours however, the reaction products were analysed and showed the same yield and product composition as in the previous case.

The catalytic base NaOH was then replaced by KO^{t}Bu (10 mol%)[283] and the catalyst loading reduced by half (0.015 mol%) as suggested by Danopoulos.[284] Substrate concentration was maintained at 2 M in propan-2-ol. Prior to addition of substrate, the

basic catalyst solution was refluxed for 45 minutes. This induction period is a common practice in order to allow the catalytically active species to be formed (*Method C*). Although not mentioned specifically in the literature, in our hands this reaction develops a blood red colour approximately 10 minutes post substrate addition with the formation of a very viscous, polymeric in appearance, material.[285] After 24 hours under reflux the reaction was cooled and quenched with either water to give a deep brown solid or with a 2 M HCl solution to yield a pale yellow precipitate. Alternatively, addition of petrol gave a red solution. Analysis of the crude products by GC revealed a mixture of *p*-tolyl alcohol, a trace of starting *p*-tolyl aldehyde and as expected *tert*-butanol. HPLC and NMR analysis demonstrated an identical product profile to that seen with the yellow oil produced by NaOH co-catalysis. The MS data were also remarkably similar, the only detectable difference between the NaOH and KO^{t}Bu promoted reactions being their colour. A 33% yield of pure alcohol was isolated from this crude reaction mixture.

A proposed mechanism for the formation of polymeric impurities involves the abstraction of a benzylic proton from the intermediate ruthenium alkoxide **154**, leading to formation of intermediate **155**. Attack on this species *p*-tolylalcohol could lead to a system primed for anionic polymerisation, Scheme 56.



n=1 m/z = 346
n=2 m/z = 450
n=3 m/z = 554

Scheme 56

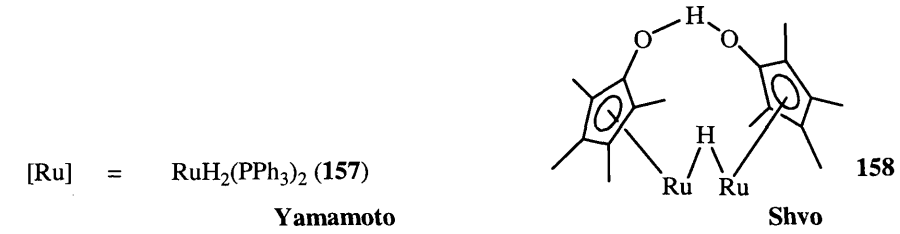
To further investigate this type of mechanism *p*-bromobenzaldehyde and benzaldehyde were subjected to the identical conditions outlined above, using KO^{t}Bu as base. The results were similar to those observed with tolualdehyde, with yields of only 25% and 31% pure products being isolated respectively, and with significant formation of red polymeric material. This effectively rules out the postulated mechanism, as there is no suitable proton to remove in order to form an intermediate like **155**. Table 3 summarises the results from the transfer hydrogenation of several substrates under these the conditions outlined above (*Method C*). 'Conversion' is indicative of how much starting material was converted to other products, be they alcohol, 'polymeric' type compounds or other products as stated, the yield indicates the amount of pure alcohol product isolated.

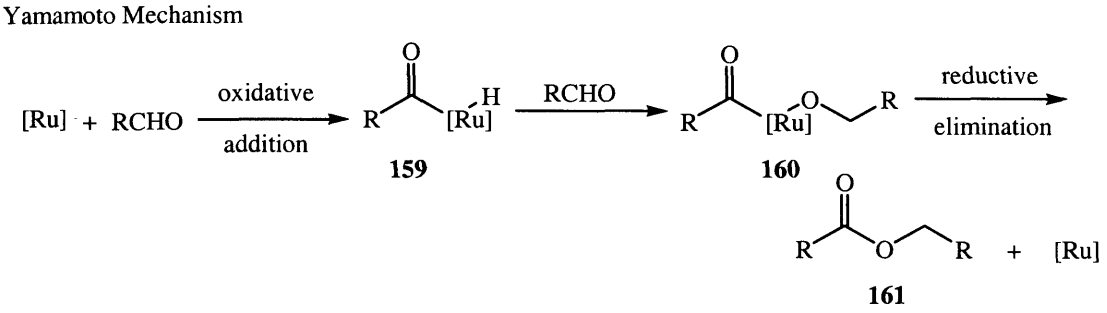
Benzaldehyde	Time (Hr.)	0.5
	Conversion (%)	100
	Yield (%)	31
p-tolualdehyde	Time (Hr.)	0.33
	Conversion (%)	100
	Yield (%)	33
p-anisaldehyde	Time (Hr.)	0.5
	Conversion (%)	100
	Yield (%)	29
p-Bromobenzaldehyde	Time (Hr.)	0.5
	Conversion (%)	100
	Yield (%)	25
Cinnamaldehyde	Time (Hr.)	2
	Conversion (%)	100
	Yield (%)	3

Table 3

In an attempt to prevent the side reaction, an experiment was carried out at room temperature using 0.015 mol% catalyst, a 0.1 M substrate concentration, and 10 mol% KO^{t}Bu (*Method D*). The reaction proceeded, but at a very slow rate and a red colour became evident in the solution. After 3 weeks, the reaction had consumed 57% of starting material, with the similar distribution of product, 'polymeric' material and starting material seen under previous conditions. The room temperature experiment was repeated, but this time replacing KO^{t}Bu with NaOH. The alternative base resulted in a minute amount of yellow oil forming on the side of the reaction vessel, and no product formation over the same time. This demonstrates the key role of the potassium cation, which is well known to have a more significant effect on the strength of the C-H bond in its alkoxides *vs.* that of the sodium counter-ion, rendering it weaker, thus accelerating the rate of transfer hydrogenation.[286]

Ruthenium catalysed disproportionation reactions involving a transfer hydrogenation type mechanism are a class of reaction that may be occurring during our reduction experiments, Scheme 57.[287]





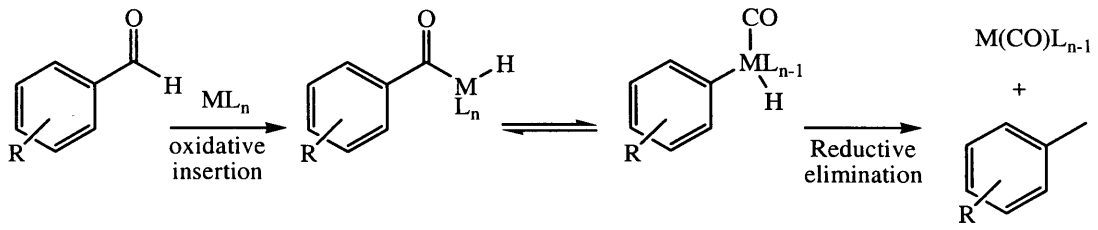
Scheme 57

In the mechanism postulated by Yamamoto (Scheme 57),[287a] an acyl ruthenium hydride **159**, formed by oxidative insertion of complex **157** into the aldehydic C-H bond of the substrate aldehyde, reduces a second molecule of aldehyde to form an intermediate acyl ruthenium alkoxide **160**, which *via* reductive elimination offers the ester **161**. Alternatively Shvo[287b] has proposed that a ruthenium hydride is necessary to reduce a molecule of aldehyde to the corresponding alcohol, which then reacts with a second molecule of aldehyde to form a hemiacetal such as **149** which is dehydrogenated by the Ru complex to yield the ester (e.g. **158**).

Disproportionation of aldehydes using Shvo's catalyst **158** gives very high turnovers for aliphatic aldehydes (TON = 19,600 for 1-methylpropanal, 5.5 hrs, 100% yield) at 60 °C, but required higher temperatures for aromatic aldehydes, for which the TON was only 4,500. There are other intramolecular based hydrogen transfer based reactions mediated by Ru (II), such as allylic alcohol isomerisations. These can proceed *via* oxidation to an intermediate ene-one system, before *in-situ* hydrogenation to give the ketone/aldehyde.[288] This particular class of reaction is not however relevant to the

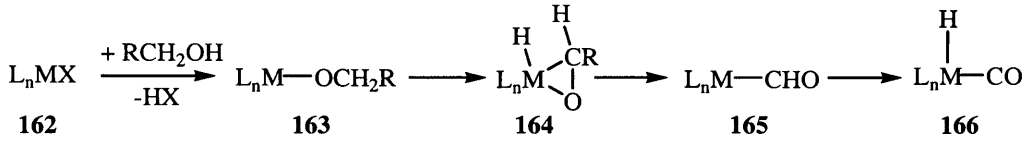
benzylic substrates which we attempted to reduce (Table 3) since there is no enolisable proton. At this stage, despite considerable experimental modification the pathway for our side reaction is still uncertain.

Aldehydes are known to be difficult to reduce[289] successfully by hydrogen transfer catalysis.[290] There are two major reasons for these complications. First, substrate decarbonylation, especially with Ir, and Rh based catalysts, may potentially poison the catalyst by transfer of a carbonyl from the aldehyde to the metal, Scheme 58.[291]



Scheme 58

Decarbonylation is common between phosphine ligated transition metal halides[292] (e.g. Wilkinson's catalyst, $RhCl(PPh_3)_3$,) and alcohols, which is the combination commonly used for the reduction of aldehydes.[293] The reaction proceeds *via* an alkoxide attack on the metal halide to give **163**, oxidative insertion then provides **164**, and a subsequent β-hydride elimination reaction leads to dehydrogenation, and finally metal carbonyl formation **166**, Scheme 59.



Scheme 59

The second reason that aldehydes are difficult substrates for transfer hydrogenation type reactions is due to the basic conditions required for the catalysis, which can deprotonate α to the carbonyl group in aliphatic aldehydes leading to aldol and related products, as well as promoting the many side reactions discussed previously.

A variety of experiments were carried out in order to try and further understand the side reaction which produced the red material. Propan-2-ol (10 mL) and *p*-tolualdehyde (20 mmol), were refluxed for 24 hours and no reaction was observed, save for a minute trace of alcohol observed *via* ^{1}H NMR. *p*-Tolualdehyde (20 mmol) and catalyst (0.03 mol%) were refluxed in propan-2-ol (10 mL) for 24 hours and again no reaction was observed. These two experiments give us some valuable information. There is no interaction between solvent, substrate or catalyst, and the reaction does not proceed without the use of a base. The fact that the reaction does not proceed without a base indicates that the complex (i.e. **111** and **112**) may well be pre-catalysts. As a blank experiment, *p*-tolualdehyde (20 mmol), KO^{t}Bu (10 mmol) and propan-2-ol (10 mL) were mixed with no ruthenium complex present. The reaction was heated to reflux (82 °C) and within 3 minutes a red colour developed, with concomitant production of the viscous, red oil. This red oil had the same NMR profile as the oil recovered when the reaction was performed previously in the presence of **111** or **112**. *p*-Tolualcohol was recovered in an identical yield to that isolated when using catalyst. The blank experiments revealed that the catalyst is not involved in the side reaction and that transfer hydrogenation can proceed, to some extent, under basic conditions in the absence of **111** or **112**. It can however be seen from a plot of alcohol *vs.* polymer formation for the catalysed and non-catalysed reaction that differences in the reaction pathway do exist, depending on whether or not the ruthenium complex is present, Figure 44.

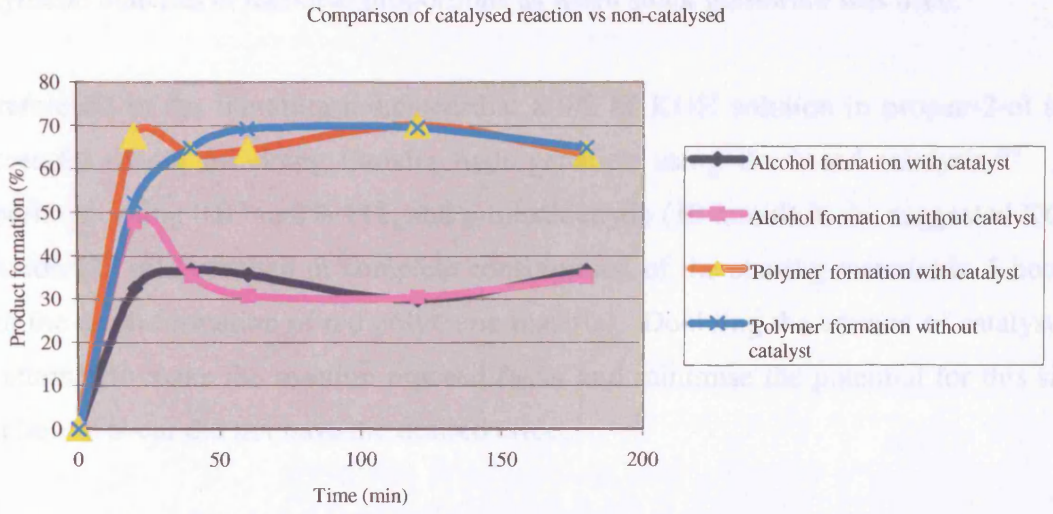


Figure 44

In the case when complex **111** is present, alcohol formation occurs at a rate approximately 0.5 times slower than polymer formation. After 40 minutes, the reaction has reached equilibrium and the ratio of alcohol:polymer remains almost constant, with the yield of alcohol at a maximum value of 36%. When there is no ruthenium complex present, alcohol and polymer formation occur at a similar rate as that of the catalysed reaction, for the first 20 minutes with the yield of alcohol reaching a maximum value of 48%. At this point there is an apparent shift in the reaction mechanism and the product alcohol appears to be consumed in a pathway that provides the polymeric type material. Consumption of the alcohol product continues for a further 40 minutes, until, 1 hour after starting the reaction, the ratio of alcohol:polymer reaches equilibrium with 31% alcohol remaining.

In order to see if these non-catalysed reactions were occurring because of residual catalyst (catalyst derivative, or unknown contaminant) remaining on the glassware after its standard cleaning procedure (base bath (KOH/propan-2-ol), acid bath, water, acetone wash), new glassware was used. Benzaldehyde and tolualdehyde were subjected to our *Method C* conditions of substrate (10 mmol), KO^{t}Bu (10 mol%) and catalyst (0.03 mol%) in propan-2-ol (5 mL) at reflux. The reaction solution developed a red colouration with formation of the insoluble polymeric material in approximately three minutes post substrate addition. After 15 minutes both reactions were analysed *via* ^{1}H NMR. The reaction mixture showed starting material, the corresponding alcohol, and polymeric material in identical proportions as when stock glassware was used.

A reference in the literature indicated that a 0.2 M KOH solution in propan-2-ol is a successful media for doing transfer hydrogenation using Ru based catalysis.[294] An experiment using 0.03 mol% **111**, and *p*-tolualdehyde (10 mmol) in the suggested KOH solution (25 mL) resulted in complete consumption of the starting material in 6 hours, with the usual formation of red polymeric material. Doubling the amount of catalyst in an attempt to make the reaction proceed faster and minimise the potential for this side reaction to occur did not have the desired effect.

It became obvious from the above experiments that the issues we were having revolved around the base in the reaction. Transfer hydrogenation reactions in propan-2-ol can be performed with between 4 – 20 equivalents of base *vs.* catalyst.[295] In our reactions,

literature precedent which recommended using approximately 350 equivalents of base *vs.* catalyst, equating to 0.1 equivalent of base *vs.* substrate (i.e. 10 mol%) was followed. In order to investigate if this large amount of base was having a deleterious effect, the amount of KO^{t}Bu was reduced to 10 equivalents *vs.* catalyst. After 60 hours at reflux, no reaction occurred, and so the amount of base was increased to 20, and then 40 equivalents.

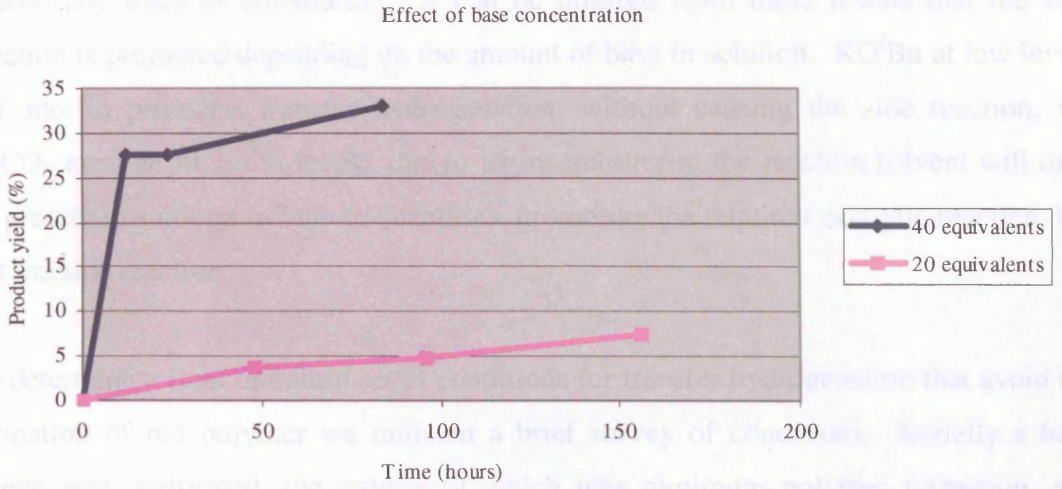


Figure 45

Figure 45 demonstrates that the number of base equivalents is critical for the successful conversion of starting aldehyde to product, with an increase in base from 20 to 40 equivalents having a significant effect on the rate of reduction. Under these conditions of reduced base concentration, there is no evidence for the side reaction that produces the red 'polymeric' material, and the reaction solution remains homogenous throughout. However these benefits are at the cost of a dramatically extended reaction time (84 hours), and a yield of only 33% of *p*-tolyl alcohol. A further increase in the number of equivalents of base initiates the alternative mechanism which produces the red material.

A suggestion from the literature indicated that potassium carbonate might be a viable base for this transformation.[296] The authors had experienced difficulties in reducing aldehydes with Ir based complexes, using KOH as co-catalyst. Potassium carbonate, a weaker base than KOH and essentially insoluble in propan-2-ol, has been applied only on rare occasions as a base for this reaction, as it has produces only a relatively small increase in the rate of the reaction in comparison to soluble bases.[297] Nevertheless we

investigated these conditions using our complex. Gratifyingly, reaction of *p*-tolualdehyde (2 mmol) and K_2CO_3 (1 mmol) in propan-2-ol (10 mL) in conjunction with **111** (0.007 mol%) gave 46% clean conversion to alcohol after 48 hours, and increasing the amount of catalyst to 0.015 mol% offered a conversion of 82% in the same amount of time. A further increase of **111** to 0.03 mol% gave 85% conversion in 24 hours, and at no time was the formation of the red polymeric material observed, or indeed any trace of colouration. It can be inferred from these results that the side reaction is promoted depending on the amount of base in solution. KO^{t}Bu at low levels (<1 mol%) promotes transfer hydrogenation, without causing the side reaction, yet K_2CO_3 even at 50 mol% levels, due to its insolubility in the reaction solvent will only be present in solution in minute quantities, promoting the required catalytic reaction, but not the side reaction.

To determine a final optimum set of conditions for transfer hydrogenation that avoid the formation of red polymer we initiated a brief survey of conditions. Initially a base screen was performed, the criteria of which was minimum polymer formation, and minimum uncatalysed reaction. The reaction screen was preformed using *p*-tolualdehyde (1 mmol), base (0.5 mmol), and **111** (0.03 mol%) in propan-2-ol (5 mL) (i.e. 0.2 M substrate concentration.) The reaction was held at reflux for 12 hours (~82°C). The catalyst, solvent and substrate were refluxed for 45 minutes before addition of base.

The bases screened were NaOH, KOH, KO^{t}Bu, K_2CO_3, Cs_2CO_3, and a control reaction with no base. A visual inspection of each reaction was sufficient to determine the successful candidate from this experiment. K_2CO_3 proved to be the most suitable base, as apart from the blank reaction all others had developed polymeric material and deep colouration. The same screen was then run with a 2.0 M-substrate concentration, and again K_2CO_3 was the most suitable base.

The next variable studied was the number of equivalents of K_2CO_3 used in the reaction. 2:1, 1:1, 0.5:1 base:substrate ratios as well as 1:1, 0.05:1 base:catalyst ratios were investigated. All other variables were maintained as stated for the base screening experiments. For the 0.2 M *p*-tolualdehyde solution, reduction was best at high base loading, 88% and quantitative conversion was seen at 1:1 and 2:1 base:substrate

respectively. For the 2.0 M *p*-tolualdehyde solution, reduction was best at 0.5:1 base:substrate loading. This gave a 66% yield of the alcohol cleanly, whereas 1:1 base:substrate resulted in a 75% yield of alcohol with concomitant formation of a significant amount of unidentified non-polymeric impurities.

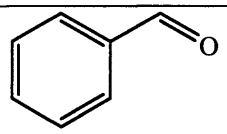
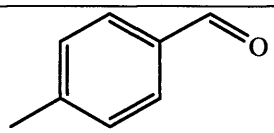
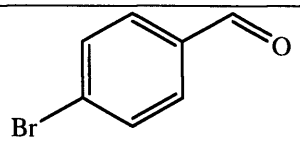
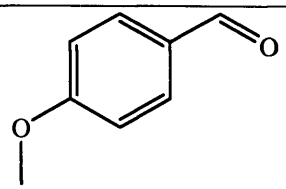
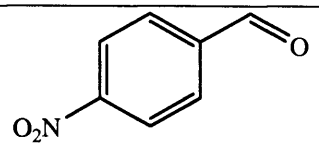
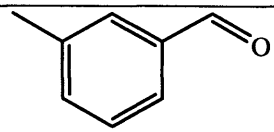
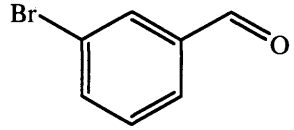
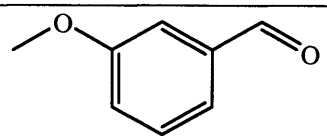
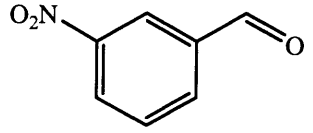
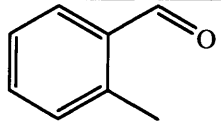
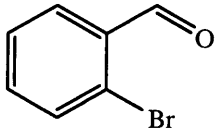
The final variable to be investigated was the incubation conditions, Table 4. All other variables were maintained as described at the outset of the experiment, with a 45-minute reflux prior to addition.

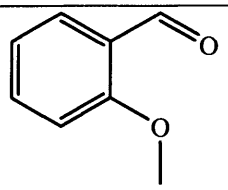
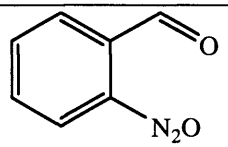
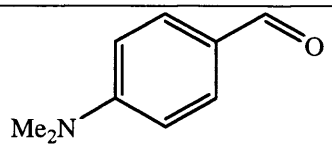
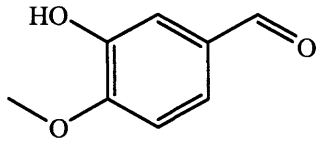
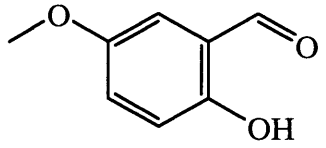
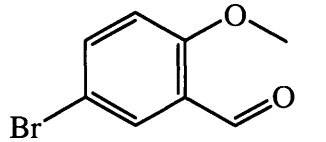
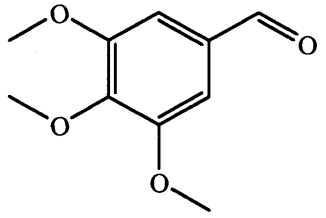
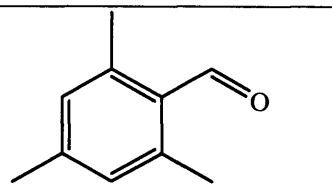
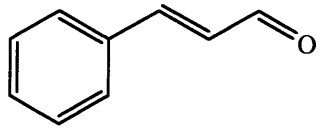
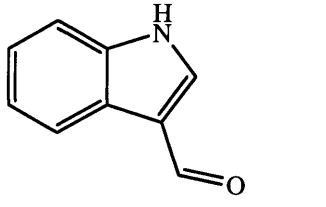
	Addition	**Yield (%) (*p*-tolyl alcohol)**
111 + solvent	Base + substrate	80
111 + solvent + substrate	Base	65
111 + solvent + base	Substrate	69

Table 4

Table 4 demonstrates that the best yield is achieved when incubating the ruthenium complex in the absence of base or substrate. This observation is similar to the findings of Crabtree,[296] who found that his ruthenium complex **88** lost activity if the activation period was performed under basic conditions. Removal of the dehydrogenated donor species (acetone) was not necessary to complete the reaction and did not influence the rate or yield significantly. Clearly the excess propan-2-ol drives the reaction by mass action.

In summary, the best results were achieved by refluxing the catalyst (0.03 mol%) in propan-2-ol (0.2 M substrate concentration) for a 45-minute incubation period, after which the substrate (1.0 eq) and K_2CO_3 (0.5 eq) are added (*General method for the reduction of aldehydes in propan-2-ol*). A range of aldehydes was then exposed to these conditions for 12 hours at reflux. The yield quoted in Table 5 is the average value for a minimum of two runs.

Substrate		Isolated Yield/%
Benzaldehyde **167**		96
p-tolualdehyde **168**		78
p-Bromobenzaldehyde **169**		100
p-anisaldehyde **170**		97
p-Nitrobenzaldehyde **171**		66
m-tolualdehyde **172**		80
m-Bromobenzaldehyde **173**		94
m-anisaldehyde **174**		82
m-Nitrobenzaldehyde **175**		61
o-tolualdehyde **176**		100
o-Bromobenzaldehyde **177**		95

o-anisaldehyde **178**		86
o-Nitrobenzaldehyde **179**		59
4 - (dimethylamino)benzaldehyde **180**		97
3-hydroxy-4-methoxybenzaldehyde **181**		38
2-hydroxy-5-methoxybenzaldehyde **182**		1
2-methoxy-5-bromobenzaldehyde **183**		71
3,4,5-trimethoxybenzaldehyde **184**		78
Mesityl aldehyde **185**		100
Cinnamaldehyde **186**		Decomp.
1*H*-indole-3-carbaldehyde **187**		0

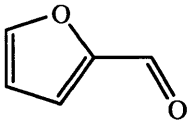
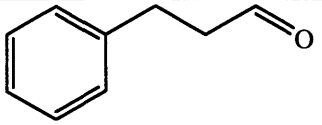
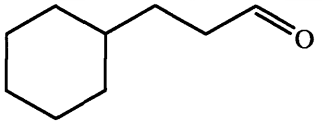
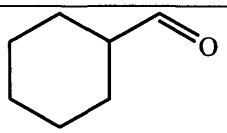
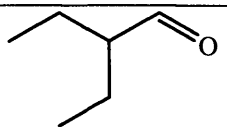
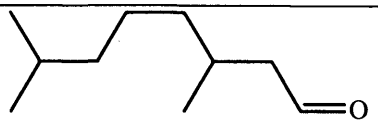
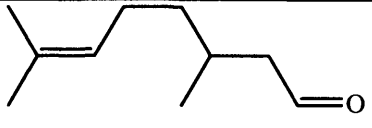
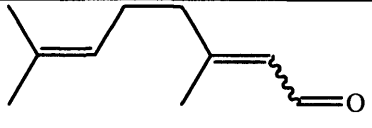
furan-2-carbaldehyde **188**		15
Hydrocinnamaldehyde **189**		89
3-cyclohexylpropanal **190**		94
Cyclohexylcarbaldehyde **191**		96
2-ethylbutanal **192**		0
3,7-dimethyloctanal **193**		75
3,7-dimethyl-6-octeneal **194**		65
(Z)/(E)-3,7-dimethylocta-2,6-dienal **195**		Decomp.

Table 5

In order to determine if there was a significant background reaction a selection of compounds was exposed to the reaction conditions (*General method*) in the absence of any catalyst, Table 6.

Compound	**Alcohol yield (24 hours)**	**Alcohol yield (48 hours)**	**Alcohol yield (96 hours)**
p-methoxy benzaldehyde	0%	0%	0%
p-Bromobenzaldehyde	0%	0%	0%
3,7-dimethyloctanal	0%	0%	0%

Table 6

Table 6 demonstrates that background reduction using K_2CO_3 (*General method*) does not occur.

4.2.3 Interpretation of the results observed during the development of methodology for the reduction of aldehydes *via* transfer hydrogenation in propan-2-ol

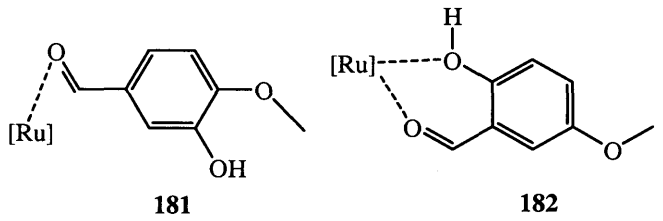
The clean, high yielding results we have seen for the reduction of aldehydes using propan-2-ol/K_2CO_3 stands in contrast to those normally reported in the literature, where they are notorious for being problematic.[298]

The difficulties in reducing aldehydes under propan-2-ol/soluble base conditions are generally related to one of the many base promoted side reactions that are possible, and application of an insoluble base, has, in our experiments suppressed these reactions. Aldehydes are more electrophilic and hence having a higher hydride affinity, are easier to reduce both thermodynamically and kinetically (less steric hindrance to hydride transfer) than ketones and imines. They react readily with ruthenium hydride species such as *cis*-$RuH_2(PPh_3)_4$ at 20 °C,[299] and with the more electron-rich *cis*-$RuH_2(PMe_3)_4$ at −20°C.[300] For complexes with labile, monodentate ligands such as $Ru(H)_2(H_2)(PPh_3)_3$, there is often the unwanted formation of ruthenium carbonyl compounds by decarbonylation from the aldehyde.[301] NHC's bind to the metal centre in an almost irreversible manner, permanently occupying coordination sites of the metal, unlike phosphines that are able to associate and disassociate under quite facile conditions, leading to the coordinatively unsaturated metal species. It is the coordinatively unsaturated complex that is capable of undergoing the CO abstraction reaction with aldehydes, and is possibly one of the reasons why NHC complexes such as those we have produced, minimise this unwanted side reaction.

112 appears to be unaffected by the electronic density of the aldehyde being reduced. When some very electron rich aldehydes are exposed to the conditions for example 4-(dimethylamino)benzaldehyde **180** (97%) or 3,4,5-trimethoxybenzaldehyde **184** (78%), the results are excellent. If we look at electron deficient aldehydes such as the nitro-substituted range of substrates **171**, **175** and **179**, the yields although slightly lower, are still very good (59-66%).

In terms of efficiency, the complexes are tolerant to steric bulk under propanol/K_2CO_3 conditions. Whilst increasing steric hindrance around the carbonyl group does lead to a slightly reduced yield, it is not significant, presumably due to the assistance of the acetone ligand maintaining a suitable sized cavity (*vide infra*) to allow substrates access to the ruthenium atom. The very hindered mesityl aldehyde **185** is reduced quantitatively, a range of *ortho/meta-* substituted aryl ketones are also all reduced in particularly good yields. These complexes (**111** and **112**) are not just applicable for the reduction of aryl aldehydes, many cyclic and acyclic aliphatic aldehydes, of various electronic and steric bulk (**186** - **195**) were reduced in high yield as detailed in Table 5.

Limitations of this method, for the reduction of aldehydes, have however become apparent. Molecules containing an alcohol, amine or a functional group capable of chelating strongly to the metal centre are not tolerated, for example 2-hydroxy-5-methoxybenzaldehyde **182** is reduced in only 1%. Comparison of this yield to that of the regioisomer i.e. 3-hydroxy-4-methoxybenzaldehyde **181**, which is reduced in 38%, provides us with an insight to the reason behind this limitation. Phenolate anion formation and chelation can combine to prevent reduction in the case of 2-hydroxy-5-methoxybenzaldehyde **182**. Both molecules posses a free hydroxyl group, however the hydroxyl functionality of 3-hydroxy-4-methoxybenzaldehyde **181** cannot coordinate to the metal centre and form a chelate as it would require the formation of a *trans* cycloheptene ring, Figure 46.



181 **182**

Figure 46

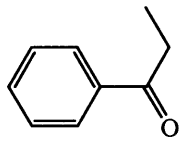
The disappointing results of 1*H*-indole-3-carbaldehyde **187** may also be explained by its chelation to the ruthenium centre *via* its nitrogen atom, preventing reduction occurring. Furan-2-carbaldehyde **188** is reduced in poor yield and we postulate that this is due to the competitive chelation of the furyl oxygen rather than the aldehyde oxygen to the ruthenium centre.

It is also interesting to note that a range of aliphatic aldehydes (**190** – **195**) were also successfully reduced, the exception being 2-ethylbutanal **192** for which, apart from the possible reason of volatility, there is no apparent explanation. α, β-unsaturated aldehydes such as citral **195** are clearly very poor substrates.

4.2.4 Propan-2-ol based conditions for ketones

In order to further explore the scope of the transfer hydrogenation reaction using the pincer complexes in propan-2-ol, the method was applied to a variety of ketones. In contrast to the behaviour with aldehydes, we had some successful results with ketone reductions using KO^{t}Bu (10 mol%), a catalyst loading of 0.03 mol% and a 2 M substrate concentration in propan-2-ol (*Method C*). Prior to addition of substrate the solution was refluxed for a 45-minute induction period.

The reduction of a ketone in propan-2-ol, using an alkoxide base, does not result in the 'polymeric' product formation observed with the reduction of aldehydes. We studied the effect of refluxing propiophenone **196** (20 mmol) in the absence of any metal complex in propan-2-ol (10 mL), with KO^{t}Bu (10 mol%). This 'blank' reaction was performed in new glassware similar to the blank experiment with aldehydes, in order to ensure that no contamination of the equipment with potential catalytic species was possible.



196

Figure 47

It demonstrated that the background transfer hydrogenation reaction does occur, but is slower than that observed for aldehydes. The plot below (Figure 48) demonstrates the extent to which the background reduction occurs, with an initial rapid rate whereby approximately 20% reduction is observed over the first 10 hours, gradually slowing down, but with 'uncatalysed' reduction still occurring after 90 hours.

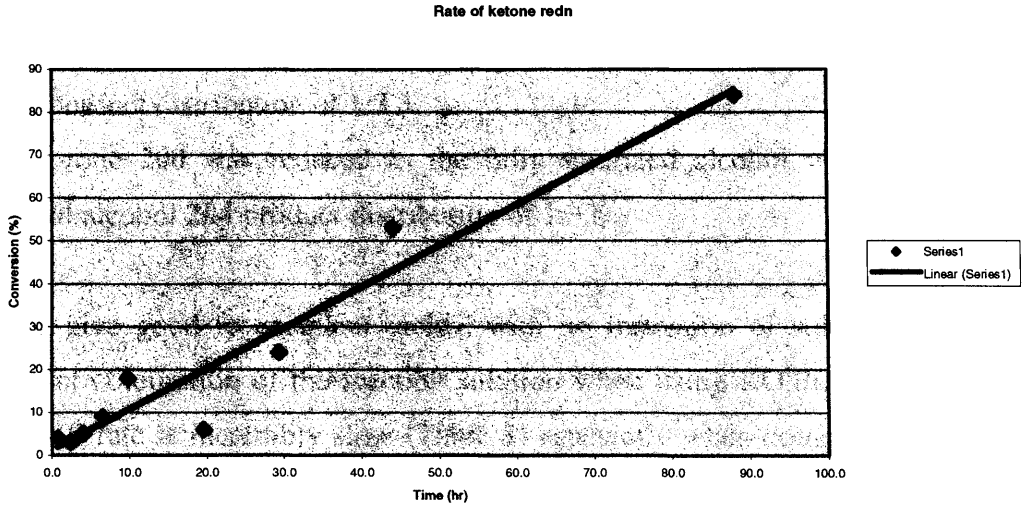


Figure 48

Using these conditions a small set of ketones was reduced. The results are summarised in Table 7.

Acetophenone **197**	Time (Hr.)	48
	Conversion (%)	100
	Yield (%)	67
Propriophenone **196**	Time (Hr.)	48
	Conversion (%)	100
	Yield (%)	95
*Iso*butyrophenone **198**	Time (Hr.)	96
	Conversion (%)	79
	Yield (%)	79
4-*tert*-butylcyclohexanone **199**	Time (Hr.)	24
	Conversion (%)	100
	Yield (%)	98*
Isophorone **200**	Time (Hr.)	96
	Conversion (%)	8
	Yield (%)	5**

Table 7

* 4-*tert*-butylcyclohexanone **199** was reduced to give an axial **201** to equatorial **202** alcohol product distribution of 1:3.3

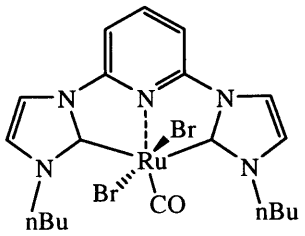
Isophorone **200 was reduced to the fully saturated alcohol with an axial **203** to equatorial alcohol **204** product distribution of 1:3.6

Ketones give good to excellent yields, with no formation of side products, or even significant colouration of the reaction solution when using KO^{t}Bu as base. However, the overall rate is incredibly slow (Table 8) especially when compared to the diamine supported ruthenium catalysts of Noyori, who, at room temperature achieves 95% yield with 97% e.e., in 10 hours, with a substrate such as acetophenone.[302] Of particular note however is the fact that the catalysed reaction is not much faster than that of the measured background reaction.

Compound	**Turn over number (TON)**	**Turn over frequency (TOF)**
Acetophenone	2,233	47
Propriophenone	3,167	66
*Iso*butyrophenone	2,633	27
4-*tert*-butylcyclo-hexanone	3,267	136
Isophorone	167	2

Table 8

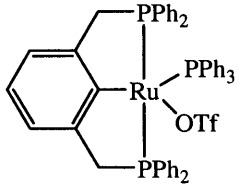
When compared to other ruthenium based pincer catalysis, such as that of Crabtree, **88** our complexes do however perform adequately.



88

Figure 49

The Crabtree complex **88** is structurally similar to our own and gives a TON of 700, with a TOF of 117 for acetophenone. However when the amount of catalyst used was reduced, a TON of 126,000, TOF 6,300 for the reduction of cyclohexanone was achieved.[303] Van Koten, using his phosphine based ruthenium pincer catalyst **205**, published results showing that the reduction of acetophenone using 0.1 mol% of catalyst can occur within 30 minutes, giving a TOF of 9,000 and a TON of 3,500.[304]



205

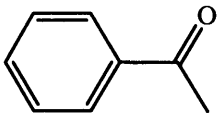
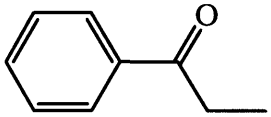
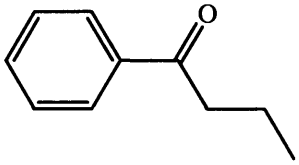
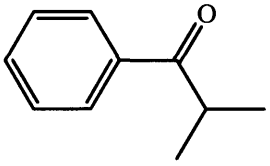
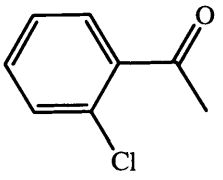
Figure 50

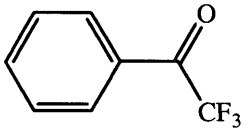
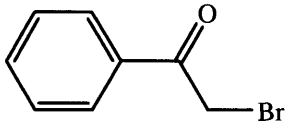
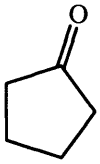
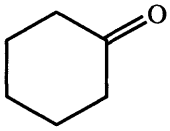
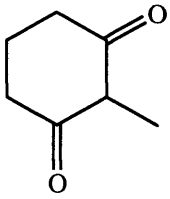
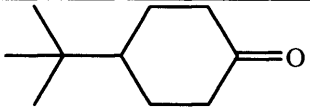
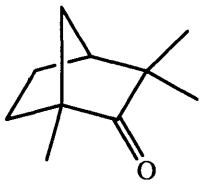
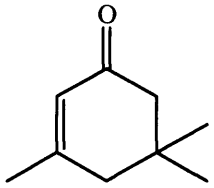
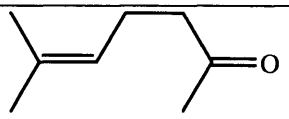
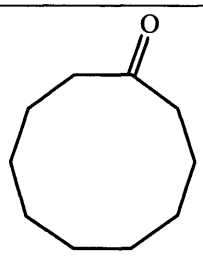
In summary, for the reduction of ketones, it can be seen that we achieve reasonable results in comparison to other ruthenium catalysts based on TON's, but our values for TOF are nevertheless comparatively small. However since the rate of the 'catalysed' reaction is just above the background rate, not a lot of value can be put on these values of TON/TOF. It is very curious indeed that the literature mentioned above does not mention any background rate, making a true comparison difficult.

In order to see if these conditions could benefit from a similar type of optimisation study that was carried out for the reduction of aldehydes, the same variables were sequentially investigated. As we have shown in Figure 48, KO^{t}Bu, causes uncatalysed reduction of the substrate. However the use of K_2CO_3 caused no background reduction

with the test substrate, acetophenone. For a 0.2 M solution of ketone and with base:substrate ratios of 2:1, 1:1 and 0.5:1 in the presence of 0.03 mol% ruthenium complex **111** yields of 66%, 64% and 67% alcohol were recovered. Lower amounts of base (1:1, 0.05:1 base:catalyst ratios) drastically reduce the yield (23%, 0% respectively). These results are surprising as we assumed that the limited solubility of K_2CO_3 would result in approximately the same amount of circulating solvated base, regardless of the amount added. This appears to have been a misguided belief, as a large excess of base *vs.* catalyst was required for a successful reaction.

In summary, the best results are achieved by refluxing catalyst (0.03 mol%) in propan-2-ol (0.2 M substrate concentration) for a 45-minute incubation period, after which substrate (1.0 eq) and K_2CO_3 (2.0 eq) are added (*General method for the reduction of ketones in propan-2-ol*). A range of ketones were exposed to these conditions for 12 hours and the yield quoted is an average of a minimum of at least 2 runs.

Substrate		**Isolated Yield/%**
Acetophenone **197**		86
Propiophenone **196**		96
1-Phenylbutan-1-one **206**		78
Isobutyrophenone **198**		81
2'-Chloroacetophenone **207**		32

2,2,2-Trifluoroacetophenone **208**		100
o-Bromoacetophenone **209**		0
Cyclopentanone **210**		80
Cyclohexanone **211**		100
2-methyl-1,3-cyclohexanedione **212**		0
4-*tert*-butylcyclohexanone **199**		100*
Fenchone **213**		0
Isophorone **200**		81**
6-Methylhept-5-en-2-one **214**		75
Cyclodecanone **215**		81

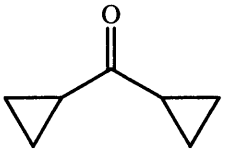
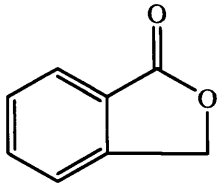
Dicyclopropyl ketone **216**		35
Phthalide **217**		0

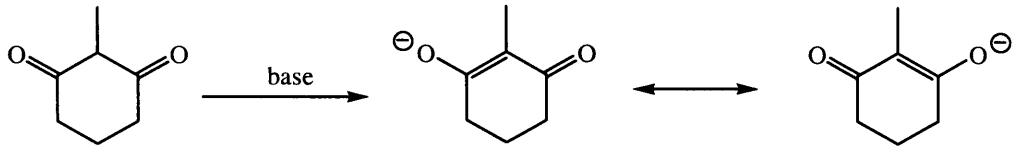
Table 9

*Compound **199** was reduced to the alcohol with a 1:2.3 ratio of axial OH **201**:equatorial OH **202** product distribution.

Compound **200 was reduced to the fully saturated alcohol with a 1:3.6 ratio of axial OH **203**:equatorial OH **204** product distribution.

4.2.5 Interpretation of the results observed during the development of methodology for the reduction of ketones *via* transfer hydrogenation in propan-2-ol

Examination of the results in Table 9 reveals that a reasonable range of aromatic, aliphatic and cyclic ketones can be successfully reduced using this protocol. Progressive increase of the bulk around the ketone allows us to determine the scope of the method. Simple alkyl-alkyl, alkyl-aryl and aryl-aryl ketones are reduced in high yields. Introducing a further degree of hindrance, as is the case of 2'-chloroacetophenone begins to affect the efficiency of the method. Dicyclopropylketone, and cyclodecanone with their bulky non-planar geometry appear to have difficulty in reaching the catalytic site, whilst the highly hindered fenchone is unaffected by the reaction conditions. As in the case of aldehydes however, compounds possessing acidic protons such as those present in 2-methyl-1,3-cyclohexanedione **212** are poor substrates. This is due to the basic conditions of the reaction giving rise to the enolic form (e.g. **218**).

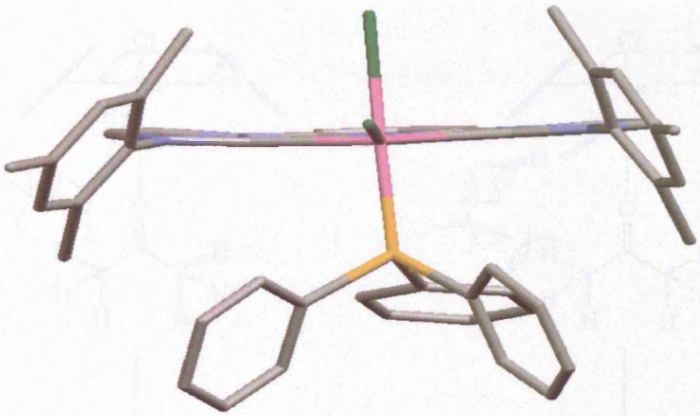


212 **218**

Scheme 60

The ketonic character of the γ-lactone phthalide **217** is insufficient to permit reduction. The successful reduction of the acyclic α,β-unsaturated ketone isophorone **200** under these conditions to the fully saturated alcohols **203** and **204** is noteworthy.

Reduction of 4-*tert*-butylcyclohexanone gives us further information on how the ruthenium complex interacts with substrates. We see consistent enrichment of the stereoisomer that is usually the more difficult to access due to the hydride source interacting with the bulky axial *tert*-butyl group. The preponderance for formation of the equatorial alcohol product, by delivery of an axial hydride can be understood by looking at the X-ray structural data for the various complexes.



111

Figure 51

Should the substrate approach the ruthenium centre with the bulky *tert*-butyl group pointing away from the disassociating acetone (or triphenylphosphine) ligand (A, Figure 52), in the direction where the only hindrance it encounters will be from the hydride or the distant aryl wingtips, it is much easier for the carbonyl to approach and coordinate with the vacant coordination site provided by the disassociating acetone ligand. If the substrate is rotated 180° along on an axis that bisects the carbonyl and *tert*-butyl bonds, a second possibility is presented (B, Figure 52). This approach would have the *tert*-butyl group interacting with the departing acetone ligand to a much greater extent making it more difficult for the carbonyl to assume a trajectory that will allow it to gain a suitable orbital overlap with the ruthenium.

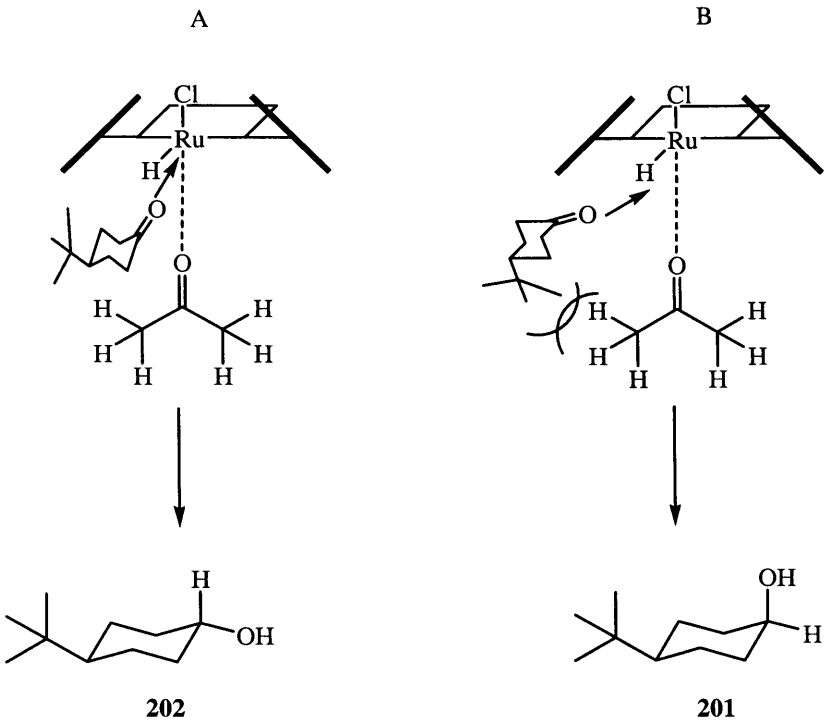


Figure 52

This steric argument explains the relatively low levels of axial alcohol **201** and justifies the preponderance of equatorial alcohol **202** isolated from the reaction product. To further investigate the enrichment of equatorial alcohol product **202** we investigated whether the enrichment may be due to a thermodynamic effect, i.e. that the axial alcohol **201** is formed under kinetic control and this then equilibrates under the reaction conditions to give the more stable di-equatorial alcohol **202**. The epimerisation equilibria of **201** to **202** has been investigated and studied for many years. It has been demonstrated to occur under conditions commonly used for MPV type transfer hydrogenation.[305] This epimerisation occurs by re-oxidation of the kinetic product then subsequent reduction, leading to the thermodynamic species, with eventual complete

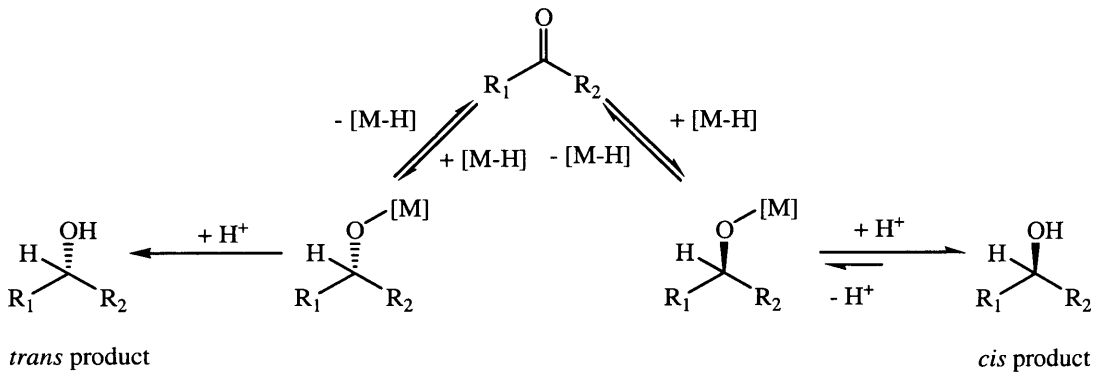


Figure 53

conversion of the reaction mixture to the more stable alcohol **202** (Figure 53) and is to be expected.[306] Exposure of both isomers of 4-*tert*-butyl alcohol to the conditions outlined in the *general method for the reduction of ketones in propan-2-ol*, for 12 hours resulted however, in recovery of unreacted starting material in each case. This is evidence to show that the enrichment we observe is induced by the catalyst alone and not due in the first instance to thermodynamic equilibration.

4.2.6 Formic acid based conditions for transfer hydrogenation of aldehydes

Our attention was then directed towards the use of non-basic conditions, and in particular the use of formic acid as the 'hydrogen' source. Transfer hydrogenation using formic acid as the hydrogen donor[307] is a valuable alternative to traditional hydrogenation with hydrogen gas.[308] The reverse reaction, the reduction of carbon dioxide to formic acid, is of great economic and ecological importance,[309] and the development of heterogeneous catalysts for this reversible reaction is of particular interest for industrial processes. In terms of its electronegativity, hydrogen occupies a central position in the periodic table. According to Pauling's definition of electronegativity,[310] hydrogen is assigned a value of 2.1, between that of fluoride (4.0) and many metals, which generally lie between 0.9 – 1.5. Therefore, a hydrogen may be transferred as a proton, atom, or a hydride depending on the reagents and conditions employed, with formic acid being generally regarded as a source of a proton and a hydride. For efficient hydrogen-donation it has been demonstrated that compounds containing hydrogen bonded to elements or groups with similar electronegativity to that of hydrogen itself, act as the best hydrogen donors. In this respect, formic acid and its formates, phosphinic acid, phosphinates, phosphorous acid, phosphites, hydrazine, hydrides of boron, aluminium, silicon, and tin, alcohols, amines, and hydrocarbons have all been applied as hydrogen donors in catalytic transfer reduction.[311] An added advantage is gained when the products of the decomposing donor have large negative enthalpies of formation. Thus, CO_2 from formic acid[312] and N_2, from hydrazine[313] provide added driving force to the reactivity of these substances as hydrogen donors.

In the event however, the reaction of complexes **111** and **112** (0.015 mol%) in formic acid (solvent) at reflux for 50 hours with *p*-tolualdehyde (*Method E*) generated no alcohol as evidenced by NMR spectra, and doubling the catalyst loading to 0.03 mol%, still resulted in no conversion.

A variation of this formic acid process is to have a 5:2 (mol/mol) solution of formic acid:TEA as the hydrogen source.[314] Alkyl ammonium formates, in particular triethylammonium formate, as it does not sublime from the reaction mixture at elevated temperatures unlike ammonium formate, have proven to be useful sources of hydrogen,

due to their solubility in organic solvents.[315] This reagent combination (*Method F*) in the presence of either **111** or **112** proved to be slower than propan-2-ol in reducing *p*-tolyl aldehyde. The reaction was held at 90 °C during the experiment and included a 45 minute induction period, in analogous fashion to that adopted for the propan-2-ol conditions.

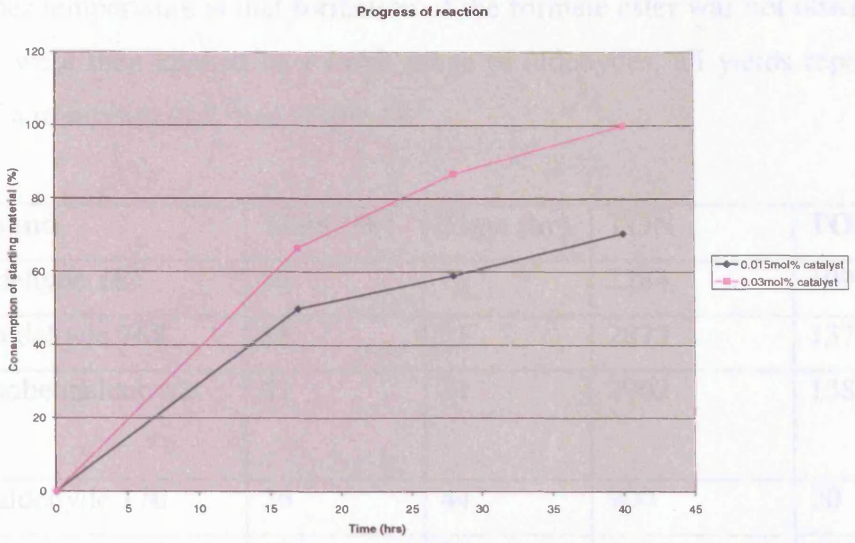


Figure 54

The data in Figure 54 clearly shows the rate acceleration attributable to the double catalyst loading. It also shows a rapid conversion of substrate during the first 20 hours of the reaction, followed by a more sedate conversion rate, but still demonstrating significant activity after 40 hours.

A critical point to note however is that this reaction, although reducing aldehydes cleanly without the development of strong colouration or polymeric type material, produces a mixture of the required alcohol and the corresponding formate ester. This problem is easily over come during the workup. Removal of volatiles and reflux of the residue in methanol, yields the desired product and volatile methyl formate. Purification by recrystallisation of the alcohol from petroleum spirit (60 °C to 80 °C) when possible or by column chromatography results in analytically pure alcohol (E.g. *p*-tolualcohol, 63%).

In order to try to improve the formic acid/TEA conditions, the reaction was then performed at reflux (150 °C). Gratifyingly, after only 21 hours the model system (*p*-tolualdehyde) had gone to completion, when using 0.03 mol% complex **111**, with substrate (10 mmol), in formic acid/TEA 5/2 azeotrope (1 M, 10 mL) (*General method for the reduction of aldehydes using a formic acid/TEA azeotrope*). A second advantage of the higher temperature is that formation of the formate ester was not observed. These conditions were then applied to a small range of aldehydes, all yields reported are an average of a minimum of 2 runs, Table 10.

Compound	**Yield (%)**	**Time (hr)**	**TON**	**TOF (hr^{-1})**
Benzaldehyde **167**	66	21	2284	109
p-Tolualdehyde **168**	83	21	2873	137
p-Bromobenzaldehyde **169**	81	21	2902	138
p-Anisaldehyde **170**	26	44	900	20
o-Tolualdehyde **176**	90	21	3115	148
o-Bromobenzaldehyde **177**	100	21	3461	165
o-Anisaldehyde **178**	47	21	1627	77
Cinnamaldehyde **186**	38* (51)	36	1315 (1765)	37 (49)

Table 10

* A further 13% of fully reduced material (hydrocinnamyl alcohol) was also isolated.

As in the case of the basic propan-2-ol protocol, an experiment was also conducted to determine the effect of the formic acid/TEA system on the substrates without the presence of any catalyst. It was observed that a slow (relative to the catalysed reaction) conversion of the aldehyde to the alcohol occurred, Figure 55.

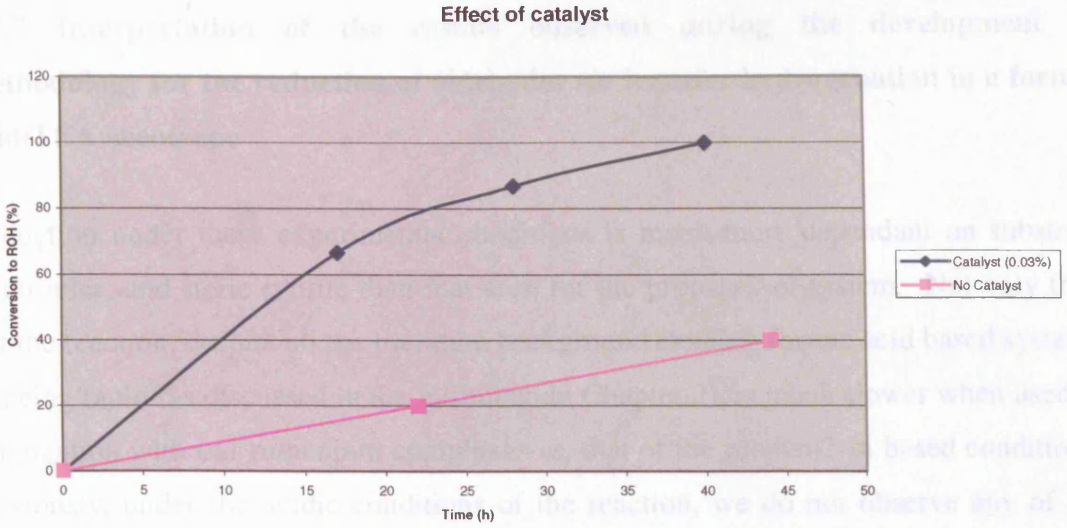


Figure 55

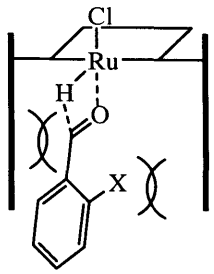
In order to assess the maximum TON, further reactions were done progressively decreasing the amount of complex with the best result achieved utilising just 0.015 mol% **111**, for the reduction of *p*-bromobenzaldehyde, giving a TON of 6235 and a TOF 283, after 48 hours, equating to just 2.25 mg of catalyst for 2.50 g of starting aldehyde. Using 0.0075 mol% of catalyst resulted in a rate of catalysis identical to that of the background and so it can be assumed that at this level that complex is not effective.

4.2.7 Interpretation of the results observed during the development of methodology for the reduction of aldehydes *via* transfer hydrogenation in a formic acid/TEA azeotrope

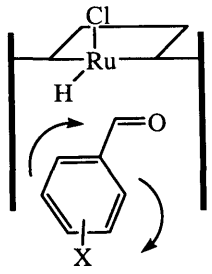
Reduction under these experimental conditions is much more dependant on substrate electronics, and steric profile than that seen for the propan-2-ol system. Not only this, but the reaction, despite all the literature background exalting formic acid based systems as being rapid (as discussed in the introduction Chapter 2), is much slower when used in conjugation with our ruthenium complexes *vs.* that of the propan-2-ol based conditions. Obviously, under the acidic conditions of the reaction, we do not observe any of the base promoted side reactions that were discussed during the development of propan-2-ol based methodology (Section 4.2.3).

Mildly electron deficient/enriched substrates are tolerated (*p*-tolualdehyde, *p*-bromobenzaldehyde), however further increasing the electronic density of the ring and hence reducing the electrophilicity of the carbonyl group drastically effects this reduction. Thus, *p*-anisaldehyde is reduced in only 26%, *vs.* 81% and 83% for the corresponding methyl and bromo-substituted benzaldehydes respectively.

The regiochemistry of substrates also has a notable effect on reductions under formic acid conditions. Without exception, reduction of substrates with *ortho* substituents (**176** - **178**) occurred in higher yields than the *para* substituted analogues (**168** - **170**), but the reasons for this trend are not clear. However, it may be due to the aryl wingtips directing the molecule into a suitable geometry for the hydride delivery to occur in an analogous manner to a molecule docking in a receptor site (Figure 56) of e.g. an enzyme. The positioning of the molecule in a suitable orientation for rapid delivery of hydride means the TOF is increased and the reaction is complete before the catalyst begins to lose activity. This optimised positioning of the molecule is only possible with *ortho* substituents since alternative regioisomers cannot benefit from the directional interaction between the ligand and the molecule since the functional groups are more remote from the wingtips.



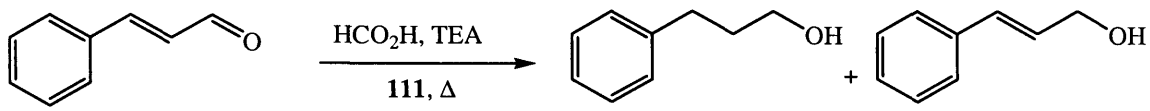
ortho substituent guiding the molecule into position giving optimum overlap between Ru and carbonyl unit



molecule free to rotate in any direction, no guiding influence on carbonyl orientation

Figure 56

The α, β-unsaturated compound cinnamaldehyde **186** was reduced in average yields under the formic acid azeotrope conditions, with a mixture of fully reduced compound **219** (13%) and allylic alcohol **220** (38%) being isolated, Scheme 61.



186 **219**, 13% **220**, 38%

Scheme 61

This is probably indicative of competitive coordination between the alkene and the carbonyl unit for the vacant coordination site on the ruthenium and hence competitive reduction.[334d] It also suggests that the 1,4-reduction of the activated double bond is disfavoured relative to C=O reduction, which is the reverse of general trends seen in hydrogen transfer catalysis.[316]

4.2.8 Formic acid based conditions for ketones

We then turned our attention to the reduction of ketones under the formic acid conditions, using 0.03 mol% complex **111**, with substrate (10 mmol), in 10 mL reaction solution (1 M). The results however, were very disappointing, Table 11.

Compound	**Yield (%)**	**Time (hr)**	**TON**	**TOF (hr^{-1})**
Acetophenone **197**	13	96	432	5
Propriophenone **196**	10	96	332	3
Isobutyrophenone **198**	0	96	N/A	N/A
4-*tert*-butylcyclohexanone **199**	86	44	2855	65
Isophorone **200**	0	96	N/A	N/A

Table 11

NMR analysis of the reaction mixture from the reduction of **199** showed that there is a mixture of four compounds. The distribution of these products is detailed in Table 12 below. The crude mixture was treated in refluxing methanol for 12 hours in an attempt to deformylate, but to our surprise, was not completely successful in this Table 12.

	Free alcohol		**Formate ester**	
	Axial **201** (%)	Equatorial **202** (%)	Axial **221** (%)	Equatorial **222** (%)
Crude	12.2	35.0	19.6	33.2
Post MeOH reflux	13.2	41.5	18.9	26.4

Table 12

Ketone reduction under the formic acid/TEA conditions was then attempted using progressively larger loadings of catalyst. No reaction was seen even with 5 mol%. A possible explanation for the unreactivity of this method is detailed in section 4.3.2, a section which compares and contrasts the difference between the propan-2-ol methods and the formic acid based methods.

To conclude, the transfer hydrogenation of aldehydes using a formic acid/TEA azeotrope is successful, but ketones, apart from 4-*tert*-butyl-cyclohexanone are unreactive. This can however be viewed as an advantage to a method. The ability to selectively reduce an aldehyde in the presence of a ketone is a useful chemoselective reaction. When a 1:1 mixture of tolualdehyde **168** (20 mmol) and *iso*butyrophenone **198** (20 mmol), are exposed to the formic acid/TEA system (*general method for the reduction of aldehydes by a formic acid/TEA azeotrope*) for an extended period, the isolated products after 36 hours are as detailed in Table 13. The reaction was allowed run for such a lengthy time to demonstrate how robust this selectivity is.

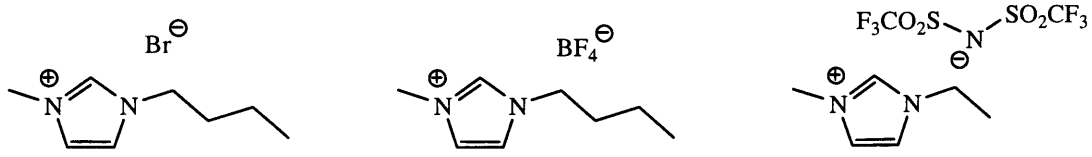
Compound	Yield (%)	Compound	Yield (%)
p-Tolualdehyde	7	*Iso*butyrophenone	45
p-Tolualcohol	43	2-Methyl-1-phenylpropan-1-ol	5

Table 13

4.2.9 Ionic liquid based conditions

There is currently a lot of interest in the use of ionic liquids in organic synthesis,[317] with the main driving force being design and implementation of 'greener' and more environmentally benign processes.[318] The unique physicochemical properties profile of ionic liquids - non-flammable, non-volatile, recyclable, extremely high boiling, as well as being thermally and chemically stable, make these attractive alternatives to standard volatile organic compounds (VOC's).[319] Ionic liquids possess a solubility range between that of aqueous and organic solvents, in part due to their purely ionic character. This orthogonal solubility profile allows product to be recovered cleanly after a reaction *via* aqueous or organic washes of the ionic liquid. Once purified, the ionic liquid is then suitable for reuse in further reactions, thereby minimising waste. The solubility characteristics of the liquid are easily changed by choice of the counter anion, leading to these media being applied to both non-catalytic and catalytic reactions[320] as well as to selective extraction.[321]

The ionic liquids investigated by us to determine the potential benefits of performing our transfer hydrogenation reactions were, 3-butyl-1-methyl-3*H*-imidazol-1-ium bromide **223**, 3-butyl-1-methyl-3*H*-imidazol-1-ium tetrafluoroborate **224** and 3-ethyl-1-methyl-3*H*-imidazol-1-ium bis triflamide **225**. TEA/Formic acid ((5/2 v/v) 10 equivalents *vs.* substrate) was added into the ionic liquid.



223 **224** **225**

Figure 57

The reduction of tolualdehyde (10 mmol) proceeds cleanly at 150°C, for 40 hours, with an isolated yield of 55%, 51% and 49%, when using **111** (0.03%) and 54%, 46% and 45%, with **112** (0.03%) in ionic liquid **223**, **224** and **225** (10 mL) respectively. However, although the reaction occurs and all the advantages of using an ionic liquid

are gained, the rate of reaction is much slower, approximately 50% of that seen with when using formic acid/TEA as solvent. There was very little difference in reaction yield and no difference in the rate of the reaction when varying either the ionic liquid structure or counter-ion.

4.2.10 Other ruthenium complexes

The 2,6-di*iso*propylphenyl substituted pincer complex, **112** possess a reactivity profile very similar to that of the mesityl complex, **111**. **112** consistently offers a slower reaction rate than **111**. However, increasing the time of the reaction when using **112** results in similar yields of product, some comparison data are given in Table 14.

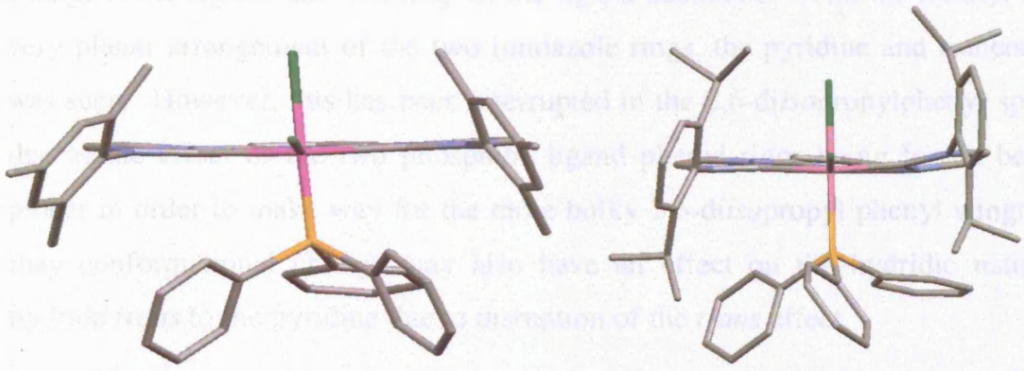
Substrate	Time (Hours)	Complex 111 Yield (%)	Complex 112 Yield (%)
Benzaldehyde	12	96	84
p-Bromobenzaldehyde	12	100	86
p-Bromobenzaldehyde	18	100	95
o-Bromobenzaldehyde	12	95	71
o-Bromobenzaldehyde	18	100	89
p-Anisaldehyde	12	97	91

Table 14

The cationic pincer complex, **114** was inactive under all sets of conditions, with the rate of reduction never greater than that seen for the background reaction.

4.2.11 Difference in reactivity profiles between the ligands

It appears that the difference in reactivity between complex **111** and **112** can be explained on the grounds of molecular conformation.



111 **112**

Figure 58

It is clear from the X-ray diffraction study that there are significant differences in the conformation of the two complexes. In the case of the mesityl species, the two wingtips are distorted from a perpendicular alignment with a very planar arrangement of the two imidazole rings, the pyridine ring and the ruthenium atom. This distortion is caused by the arrangement of the triphenylphosphine rings. Two of these phenyl rings are arranged at an angle parallel to each mesityl ring, whilst the third is pointing down and to the back of the ligand, below the pyridine ring. In the case of the di*iso*propylphenyl complex, we do not observe this very effective symmetrical packing of atoms. Rather, two of the three triphenyl phosphine rings are underneath the imidazole-pyridine scaffold, with the third ring pointing out towards the front of the ligand, directly below the chloride and *cis* to the pyridine unit. This difference has a dramatic effect on the molecular conformation. No longer does the catalyst posses an area below the metal atom for substrates to coordinate, as is the case with the mesityl ligand, as a phenyl ring from the phosphine ligand is now located in the cavity where a substrate is expected to enter. The alternative arrangement of the aryl rings of the phosphine in **112** *vs.* that of **111** is due to one of the bulky di*iso*propylphenyl rings lying perpendicular to the ligand, and the second slightly distorted away from perpendicular in order to minimise

interactions between the phosphine and *iso*propyl wingtips. The effect of this conformation is the significant reduction of the amount of space available for disassociation of the phosphine and coordination of a substrate. The possibility that the phosphine is essentially 'trapped' in position below the ligand may contribute to an understanding of the slower rate of reaction of this complex. The other key structural change is the significant 'warping' of the ligand backbone. With the mesityl species, a very planar arrangement of the two imidazole rings, the pyridine and ruthenium atom was seen. However, this has been interrupted in the 2,6-di*iso*propylphenyl species **112** due to the effect of the two phosphine ligand phenyl rings being forced beneath the pincer in order to make way for the more bulky 2,6-di*iso*propyl phenyl wingtips. This may conformational change may also have an effect on the hydridic nature of the hydride *trans* to the pyridine due to disruption of the *trans* effect.

The cationic species **114** has no outstanding structural differences *vs.* its mesityl parent **111**, implying that its inactivity is due to the altered electronic profile of the system. Cationic ruthenium transfer hydrogenation catalysts are known[322] as are their anionic counterparts.[323] In the case of the cationic species, the vast majority are Ru-arene type complexes. In our case however, the coordinated MeCN has had the effect of poisoning the catalytic activity of the complex, due to it preventing the formation of a hydride species as discussed earlier.

4.3 Further discussion of results

4.3.1 Proposed mechanism for the reaction

As discussed in the introduction, two general mechanistic pathways have been proposed for hydrogen transfer: 1) direct hydrogen transfer (A) and 2) a hydridic route (B), Figure 59.

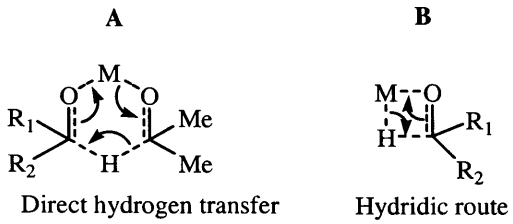
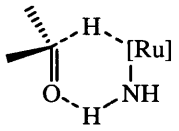


Figure 59

No ruthenium based catalytic system has yet been shown to follow a direct hydrogen transfer type mechanism, as what occurs with the traditional MPV based system.[324] Although Nyori's diamine based catalysts operate *via* a 6-membered transition state **226**, that appears initially to be similar to the MPV reaction, it is infact quite different, since it employes the concept known as metal-ligand bifunctional catalysts whereby hydride transfer from RuH and proton transfer from NH occur simultaneously, Figure 60.[325]



226

Figure 60

Ruthenium catalysed transfer hydrogenation is more likely to proceed by the hydridic mechanism. The hydrogenation of polar bonds by ruthenium hydrides involves the coordination of the carbonyl (or possibly olefin) functionality to a vacant coordination site of the ruthenium (II) centre, made free by dissociation of a ligand. Coordination allows for the electrophilic activation of the carbon atom of the carbonyl by the metal

ion so that a *cis* hydride ligand can be transferred, thereby effecting the reduction of the carbonyl unit. However, it is at this point in the mechanism that a shortfall in catalysts operating under this type of mechanism becomes apparent. Competition exists between the coordination of either a carbonyl unit or an olefin, and in an α,β-unsaturated system such as cinnamaldehyde, both possibilities can occur, leading to a mixture of reduced products, the ratio of which depends on the relative affinity of the olefin and the carbonyl for the metal centre. We observed this when subjecting cinnamaldehyde **186** to the formic acid/TEA system, with both hydrocinnamyl alcohol **219** and cinnamyl alcohol **220** being recovered. This can also explain the complete reduction of isophorone **200** to the saturated alcohol **203/204**, rather than the reduction stopping at the allylic alcohol when it was reacted under the propan-2-ol conditions.

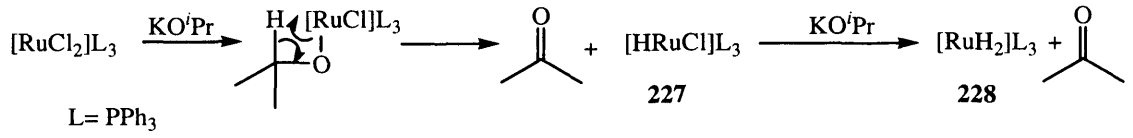
A ruthenium hydride species can be formed by oxidative insertion of the ruthenium to the OH bond of the hydrogen source,[326] or by alkoxide attack on the Ru centre, followed by a β-hydride elimination reaction.[327] We believe in the case of our catalysts, that initial formation of the ruthenium hydride from the catalyst precursors **111** and **112** occurs by this latter pathway. This belief is supported by the fact that no reaction occurs when the ruthenium complex, propan-2-ol and substrate are reacted together, and only on addition of base do we see formation of product. This is most likely due to the formation of an alkoxide, which is obviously more nucleophilic than the parent alcohol and is capable of attacking the ruthenium complex leading to displacement of a chloride (with formation of e.g. KCl). The coordinatively unsaturated ruthenium alkoxide then undergoes a β-hydride elimination to form a Ru-H species, with a molecule of acetone being formed. It is uncertain whether at this point the phosphine ligand is exchanged for acetone, which could function as an alternative supporting ligand. If an oxidative insertion process were responsible for the formation of the initial hydride, we would have observed product formation without the addition of base.

Once the metal hydride has formed, further aspects of the ligand begin to play a role on the reactivity of the species. The electron donation from the carbene ligands support the ruthenium centre during the various stages of the mechanism, to a greater extent than a phosphine ligand can. The *trans effect*[328] from the pyridine-nitrogen weakens the Ru-H bond, rendering it more reactive. This helps us to understand why the cationic MeCN substituted complex **114** is not reactive. The more tightly bound MeCN is occupying

the position *trans* to the pyridine, resulting in the axial chloride being the only available position for a hydride to form. The axial hydride will be much less reactive (if it forms in the first place), since it does not experience the *trans effect* as with the equatorial hydride of the parent complexes (**111**, **112**). Conventional nomenclature calls all complexes with a bond between a metal and hydrogen a 'metal hydride' however this does not need imply that they will exhibit hydridic reactivity. Metal hydrides exhibit a wide range of kinetic and thermodynamic acidity.[329] Measurements in MeCN, showed the pK_a of the hydride on the cobalt complex $[CoH(CO)_4]$ to be 8.3 - of comparable acidity to HCl in that solvent. The molybdenum hydride $[Mo(Cp)(CO)_3H]$ is less acidic, with a pK_a of 13.9.[330] In fact it has been established that one-electron oxidation of metal hydrides can produce super-acids, with a pK_a of -6.0 estimated in MeCN for the radical cation complex $[Mo(Cp)(CO)_3H]^{+\cdot}$.[331] For our purposes, we need a complex capable of donating a hydride, yet it is abundantly clear that such complexes can have ample acidity and perhaps the theoretical axial hydride is not of sufficient hydridic character to undergo the reaction.

An electron rich metal centre facilitates oxidative addition to, for example, an aldehyde C-H bond. Although we have the two strongly electron donating NHC ligands increasing the electron density of the ruthenium centre, they have been tempered, to some extent, by substitution with electron withdrawing aromatic rings. This diminution of their donating character may be sufficient to eliminate the possibility of an aldehyde oxidatively inserting into the complex, leading to decarbonylation. This is one of the common causes of failure for transfer hydrogenation reactions of aldehydes, mediated by transition metal catalysis.

The question of whether or not we form a mono- or di-hydride species can be speculatively answered by taking into account experimental evidence and literature background. For transfer hydrogenation reactions using $RuCl_2(PPh_3)_3$, it has been demonstrated that the dichloride **107** and the chlorohydride **227** are completely unreactive, however the dihydride **228** reacts rapidly with ketones to give the corresponding alcohol.[332] This lack of activity was observed in our own experiments when treatment of our complexes with propan-2-ol and an aldehyde or ketone at reflux led to no product formation, thus confirming that the dichloride is inactive. A dihydride species is formed *via* two iterative reactions with an alkoxide and subsequent β-hydride

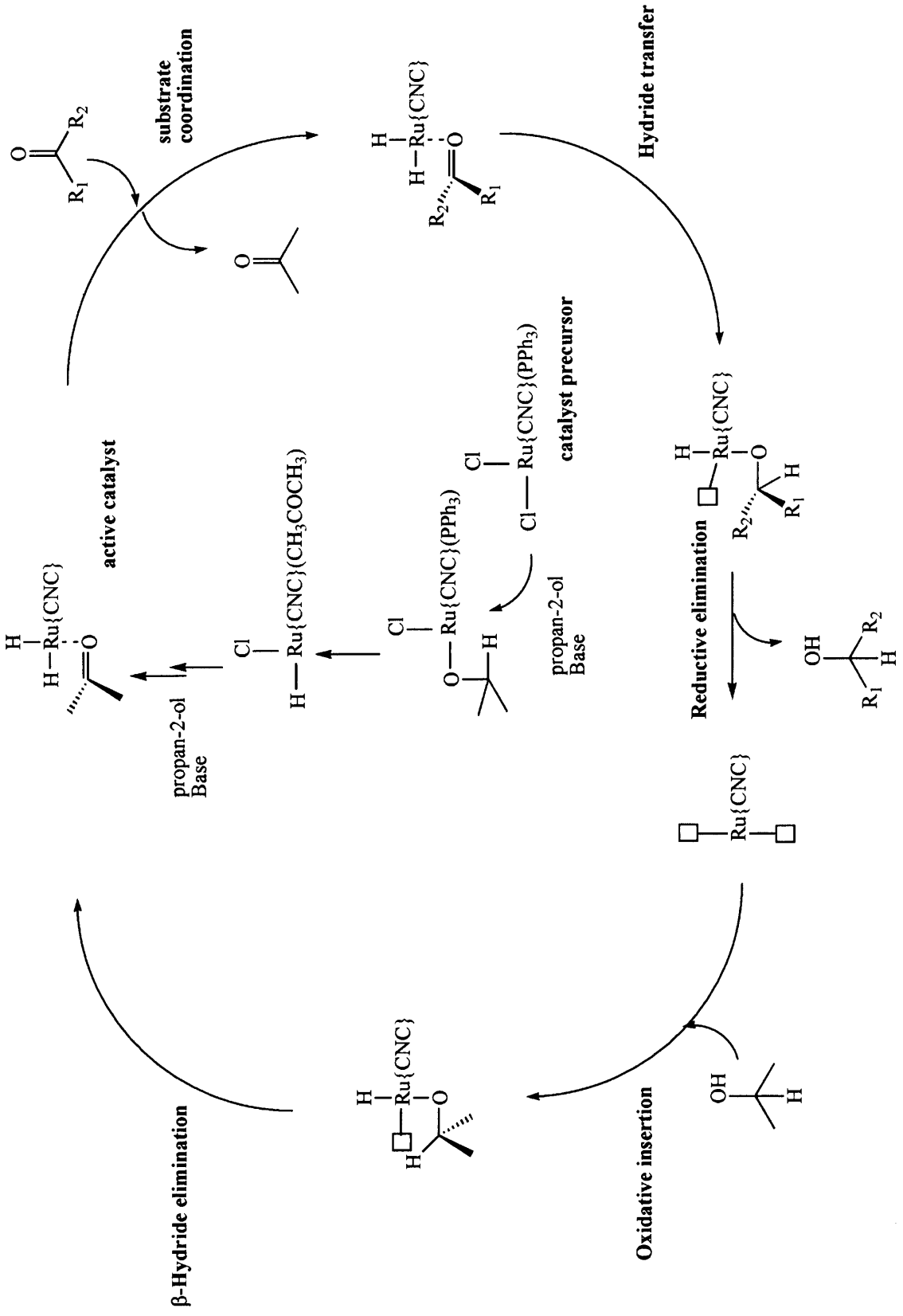


Scheme 62

elimination reactions on the ruthenium centre, Scheme 62. This is an entirely feasible mechanism as it has been proved that transition metal bound chlorides are easily replaced by hydrides, and also this has been observed to occur with $RuCl_2(PPh_3)_3$.[333] Formation of a dihydride does not necessarily occur for all Ru based catalysts, indeed it has been shown that many Ru, and the majority of Rh and Ir catalysts function by a monohydride mechanism.[334] However, since to the best approximation, our pincer complexes resemble $RuCl_2(PPh_3)_3$, we might assume that our complex forms a dihydride intermediate, analogous to the known $RuH_2(PPh_3)_3$. At this point it should be highlighted that this provides another reason for the failure of the MeCN complex **114** to be active in our transfer hydrogenation studies. Exchange of a more tightly bound MeCN *vs.* a chloride, for a hydride will be much more difficult, perhaps not occurring at all, preventing the formation of the dihydride species.

Having established that a likely mechanism involves a dihydride, the next mechanistic issue to reflect upon is the fate of the two 'hydrides' attached to the ruthenium species. Bäckvall has studied this process in detail as discussed in chapter 2 of this thesis. He established that the precatalyst $RuCl_2(PPh_3)_3$, after conversion to the active species $RuH_2(PPh_3)_3$, demonstrates no selectivity in terms of which 'hydride' is donated as an actual hydride and which is donated as a proton.[335] This is in contrast to other catalysts where there is a strong correlation between the origin of the proton and the form it takes when it is later transferred, and without detailed labelling studies it is impossible to tell in which mode our complexes transfer their hydrides. From this point onwards the remainder of the catalytic cycle is well established. Reductive elimination of the product alcohol gives us a very reactive Ru (0) species. This undergoes oxidative insertion with the O–H bond of the hydrogen donor alcohol to produce the alkoxy-hydride complex that leads back to the dihydride catalyst after a β-hydride elimination. This mechanism is consistent with many chemical, NMR and isotopic labelling experiments, along with our own experimental findings. The first proposal for a Ru (0) $(PPh_3)_3$ intermediate during transfer hydrogenation using $RuCl_2(PPh_3)_3$ was made by

Imai *et al.* whilst studying *cis*-$RuH_2(PPh_3)_4$ in bromobenzene as a catalyst for transfer hydrogenation.[336] Wilkinson, who believed Imai had used inferior quality methods to prepare his organometallic complexes, questioned the validity of this work,[337] but over time and with continued research the existence of a Ru (0) species has been confirmed and accepted as a valid intermediate in the catalytic cycle. A schematic of the complete cycle is presented in Scheme 63, where {CNC} represents the pincer ligand.



□
| = vacant coordination site / or either a PPh_3 or acetone ligand

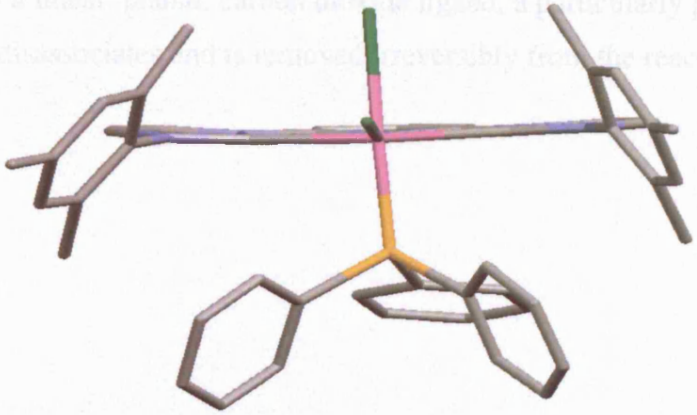
Scheme 63

4.3.2 Explanation for the selectivity differences of the propan-2-ol and formic acid methods

Since the use of formic acid based systems clearly resulted in a substantially different reactivity profile, it is also of relevance to examine the mechanistic basis for our observations.

It has been postulated that the mechanism for the formic acid/azeotrope may follow a different mechanism, whereby formic acid could be catalytically decomposed to H_2 and CO_2, and, in a second step, the H_2 is used to achieve catalytic hydrogenation of the carbonyl unit. It has been shown that catalytic hydrogenation using H_2 does occur with $RuCl_2(PPh_3)_3$, but only when in neat acetophenone, at 88 atmospheres of H_2 pressure, and 125 °C,[338] essentially ruling out the possibility that this type of mechanism could be occurring with our complexes under the experimental conditions we use.

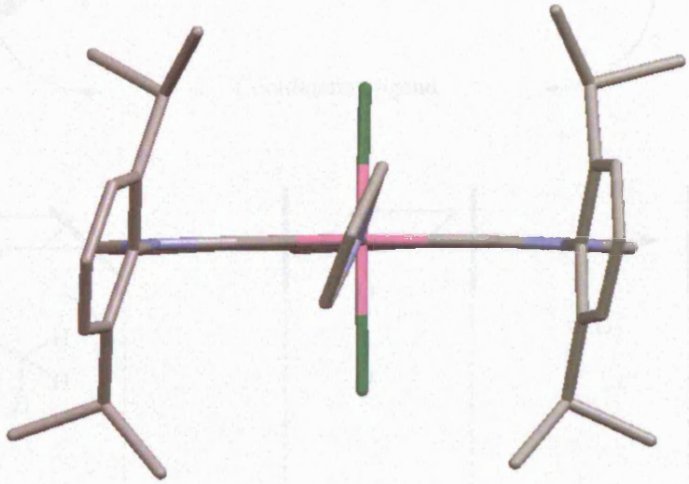
We believe that the difference in reactivity between our two sets of conditions may lie in the steric environment created immediately after formation of a hydrido species. Examination of the X-ray structure of **111/112** shows that the aromatic rings are forced to adopt an angle which is less than 180° to the axial chloride, and distorted from the 90° angle one might imagine they would form with the planar ligand. The reason for this distortion may be attributed to the aryl rings of the triphenylphosphine, interacting with the aromatic wingtips, forcing them out on the lower face of the ligand, and consequently, moving them in on the top face.



111

Figure 61

When the X-Ray structure of the pyridine substituted complex **113** is studied, this deviation in the alignment of the aromatic wing-tips is not observed, as there is no steric bulk (aryl-phosphine substituents) to interact with the wing-tips and push them out of their preferred perpendicular alignment with the rest of the planar ligand.



113

Figure 62

When a ruthenium hydride species is formed from a propan-2-ol molecule, the final outcome of the reaction results in the triphenylphosphine ligand being most likely replaced by an acetone molecule, which acts as a ligand, and remains associated to the ruthenium centre until it is displaced by a substrate molecule. When the ruthenium hydride species is formed *via* reductive elimination of formate, the bulky phosphine is now replaced by a linear, planar, carbon dioxide ligand, a particularly poor 'ligand', and as such, readily disassociates and is removed irreversibly from the reaction solution.

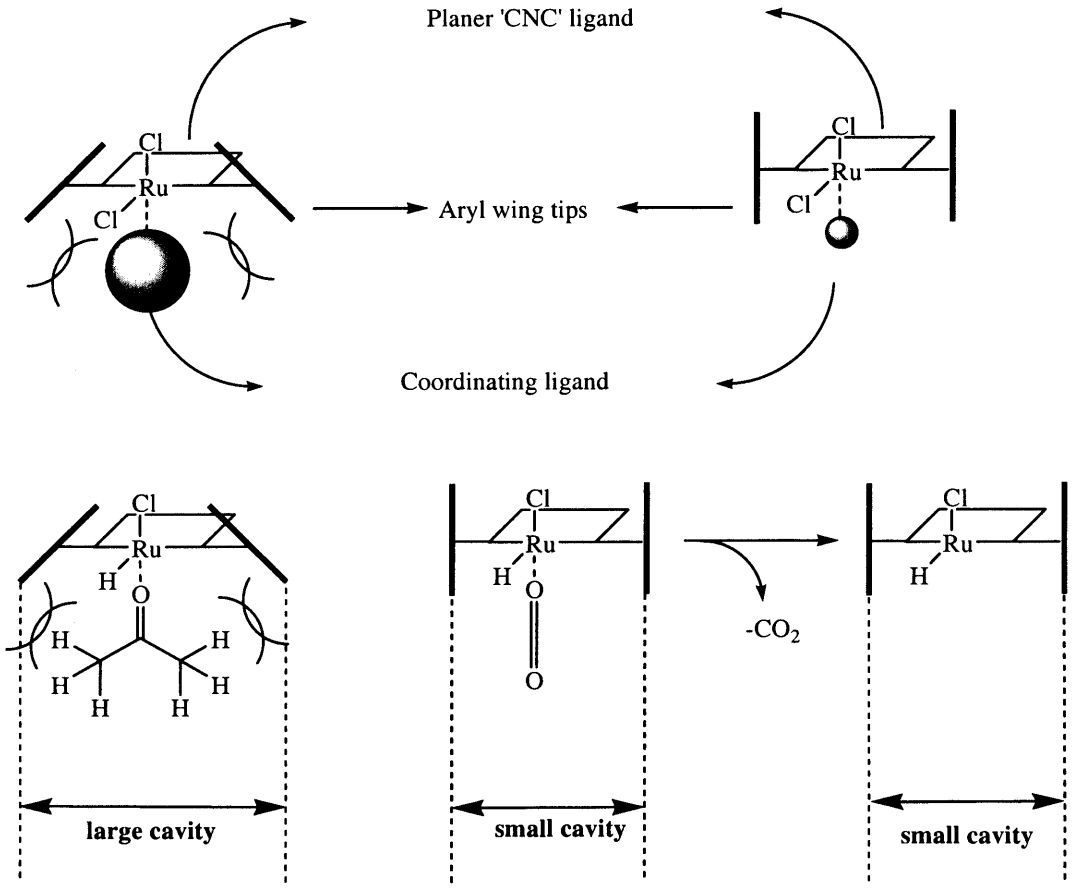


Figure 63

Figure 63 shows the proposed difference in the alignment of the aromatic wing tips. The representation of the geometry for the aryl wingtips depending on the associated ligand in this diagram, can be justified by observations made from the X-ray studies of the phosphine and pyridine ligated complexes. What becomes clear when looking at this figure is the difference in the capacity of the cavity below the plane of the ligand where our substrates are expected to associate to the metal centre. The acetone ligand, due to its relatively large steric presence, causes the wingtips to be pushed out on the lower face of the ligand, increasing the size of substrate capable of approaching the metal, without having to encounter the wingtips. When we look at the cases where we have either an associated carbon dioxide or the coordinatively unsaturated species formed by loss of carbon dioxide, we have essentially the same picture in which the linear geometry of carbon dioxide[339] results in minimal displacement of the wingtips, as is the case for the coordinatively unsaturated species. This results in the wingtips adopting a perpendicular (*vs.* the plane of the ligand) geometry, analogous to **113** seen in Figure 62, thus minimising the effective cavity for substrate approach, and thus

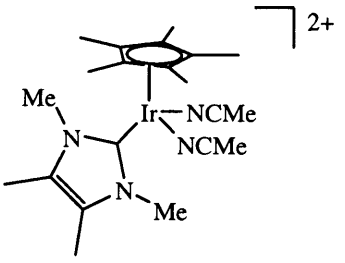
helping to explain why aldehydes with their sterically less demanding carbonyl group (RCHO) work under formic acid conditions, but not ketones whose carbonyl units posses a larger steric profile RCOR`, preventing their association to the ligated metal centre.

Chapter 5

Oxidation

5.1.1 Oppenauer oxidation

The development of environmentally benign oxidation reactions has attracted considerable attention, and many transition metal catalysed systems for the oxidation of alcohols using oxygen, hydrogen peroxide, or other oxygen atom transfer reagents as an oxidant have been reported in recent years.[340] Some transition metal catalysed systems for Oppenauer type oxidations have also been reported,[341] although a highly effective system has rarely been realised.[341e-g] Amongst the most active species are iridium ligated NHC compounds, with TON's of up to 950 recorded for secondary alcohols and 196 for primary alcohols. Until recently, these were the best available values, but Yamaguchi has now improved the TON for secondary alcohols to 3,200 using the NHC supported cationic Ir complex **229**, without however any further improvement for primary alcohols.[342]



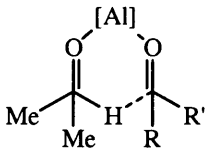
229

Figure 64

Accordingly we investigated the application of our three pincer complexes **111**, **112** and **114** in to the Oppenauer oxidation of primary and secondary alcohols. Using conditions similar to those developed by us for transfer hydrogenation (*general method for the transfer hydrogenation of aldehydes/ketones in propan-2-ol*), but using acetone as the hydride acceptor, (substrate (1.0 eq) in acetone (0.2 M), K_2CO_3 (0.5 eq), complex (0.03 mol%) with a 45 minute substrate incubation) the oxidation of tolyl alcohol was attempted (*Oppenauer type oxidation method A*), but no conversion was observed at room temperature or at reflux even after 60 hours. Increasing the amount of ruthenium complex to 5 mol% and repeating the experiments either at room temperature or at reflux still resulted in no conversion with any of the complexes.

5.1.2 Interpretation of the results observed during the development of methodology for the Oppenauer oxidation of alcohols.

As mentioned during chapter 4 on transfer hydrogenation, MPV-O type reactions catalysed by Ru have not been observed to proceed through a six membered transition state, which is the mechanism for direct hydrogen transfer and for traditional Oppenauer oxidations. This implies that a Ru catalysed Oppenauer type oxidation most likely proceeds in a manner similar to that of transfer hydrogenation, i.e. *via* initial formation of a Ru-hydride species, except that in this case it is formed by dehydrogenation of the substrate alcohol. In the case of transfer hydrogenation reactions, the solvent is responsible for creating the active ruthenium hydride so that the reaction is kinetically favoured to proceed. In the Oppenauer oxidation however, attempts to use a dilute solution of the substrate in acetone as solvent results in a kinetically disfavoured formation of the pre-requisite ruthenium hydride species. Moreover, the competitive chelation of acetone molecules (*vs.* substrate molecules) to the ruthenium centre will also reduce the rate at which substrate molecules can complex to the metal. It therefore becomes apparent why oxidation is more difficult to effect than the corresponding reduction. During our experimental investigations, we were unable to promote a catalytic oxidation using our complexes *via* an Oppenauer type reaction. When using aluminium alkoxides as in the traditional Oppenauer oxidation, it requires only one acetone and one substrate molecule to associate to the metal centre to form the active

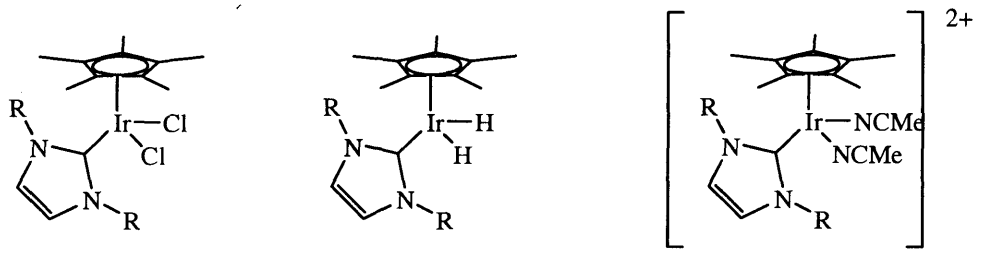


230

Figure 65

'complex' **230**. For the reaction to proceed using our Ru complexes requires firstly the successful attack of the Ru-complex by a substrate molecule, leading to formation of a hydride with concomitant formation of a molecule of product (via a β–hydride elimination process), then oxidation of the so formed Ru-hydride species must occur by hydride transfer to a molecule of acetone to complete the catalytic cycle – essentially

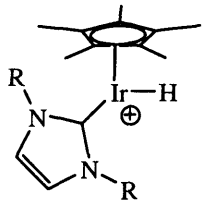
double the number of operations required for each catalytic cycle in comparison to the traditional MPV-O mechanism. One of the most successful NHC-transition metal catalysts to date, the Iridium complex **229**, was inactive in its neutral state **231** (1% yield for the reduction of acetophenone).



231 **232** **229**

Figure 66

It was only on treatment with two equivalents of **231** with AgOTf to form the doubly cationic complex **229** that it became active demonstrating a TON of 950 (95% yield for the oxidation of 1-phenylethan-1-ol).[342] Interestingly, the dihydride analogue **232**, was not active (0% yield) in the reaction and for this reason the authors believed it was not involved in the catalytic cycle. Rather, a monocationic, monohydride species **233** is



233

Figure 67

believed to be the active species.[343] Use of our monocationic species **114** was unsuccessful and no product was generated, indicating perhaps that formation of a hydride in the axial position was not possible under the reaction conditions which were attempted to affect the Oppenauer oxidation.

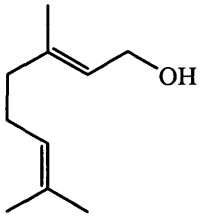
The phosphine ligated iridium species, $Cp^*Ir(PBu_3)(MeCN)_2][OTf]_2$ **234**, is isoelectronic with **229**, yet was inactive under the reaction conditions that gave

successful results with the NHC substituted iridium complex. This was attributed potentially to electronic effects, but more critically, to the much larger steric demands of the phosphine ligands that were believed to be preventing the reaction from progressing. The X-ray structure of the dicationic NHC-species shows a very accessible metal surface, unlike the hindered iridium atom of the phosphine complex or the highly sheltered ruthenium centre in complexes **111**, **112** and **114**. If the reaction requires significant space around the metal atom in order to proceed, it could well explain why our 'sheltered' Ru atom is incapable of supporting the reaction mechanism.

5.2 Stoichiometric co-oxidant promoted oxidations

5.2.1 N-Methylmorpholine-N-oxide

After establishing that our complexes are not active under traditional Oppenauer type conditions we therefore turned to alternative methods to effect oxidation. Work by Sharpless[344] on alcohol oxidation using $RuCl_2(PPh_3)_3$ in conjunction with NMO as a stoichiometric oxidant was speculated in the paper to proceed *via* a ruthenium-oxo species. In order to probe the mechanism of the reaction, we examined one of the literature examples (geraniol, **234**) in the absence of NMO, in order to check that an

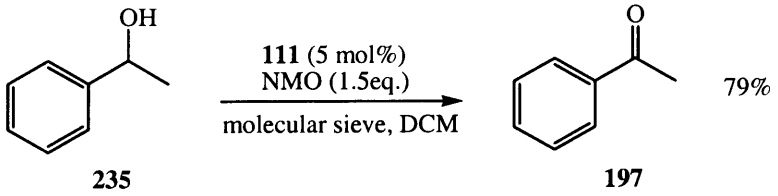


234

Figure 68

Oppenauer mechanism was not operative. The reaction initially went a golden brown colour as detailed in the paper, but rapidly turned to a bright green (*vs.* dark brown in the paper) and remained as such for the entire course of the reaction. Only a minute trace of aldehyde was detected (>1%) on workup, eradicating any belief that the mechanism is Oppenauer based. Since we believed that our complexes can function in a similar fashion to $RuCl_2(PPh_3)_3$ we decided to explore the use of NMO (anhydrous) as a stoichiometric oxidant in conjunction with the ruthenium NHC complexes, **111**, **112** and **114**

Initially the standard TPAP conditions outlined by Ley were investigated.[345] Using 1-phenylethanol **235** (1.0 eq) as a test substrate in DCM (0.2 M), with NMO (1.5 eq) **111** (5 mol%) was added together with molecular sieves (500 mg/mmol, finely ground) to the reaction solution.



235 197

Scheme 64

After 20 hours at room temperature, the reaction had proceeded cleanly with a 79% yield of acetophenone, **197**. Reduction of the catalyst loading to 0.5 mol%, resulted in a 76% yield of acetophenone after 4 days at room temperature, which is however much slower than the two hours required by either the Ley or Sharpless protocols.

We then turned to a second common set of conditions which are commonly applied to 'difficult' substrates when using TPAP, in which acetonitrile is substituted for DCM as the reaction solvent. In this case only a 19% yield of acetophenone after was isolated after 24 hours when using **111** (5 mol%) or 14% with **112** (5 mol%). These low yields could be attributed to deactivation of the catalyst by displacement of the equatorial chloride from the ruthenium forming the cationic complex, **114**. This led us to query as to whether the reduction product N-methylmorpholine, was acting as a ligand and poisoning the complexes during the reaction. Further credence was given to this supposition following the observation that the cationic MeCN substituted complex **114** was inactive under conditions which resulted in successful oxidations for both **111** and **112**.

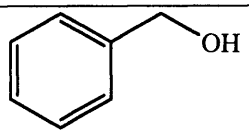
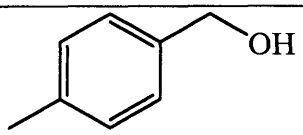
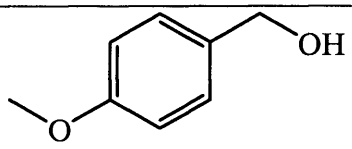
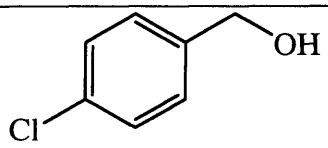
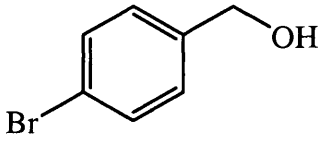
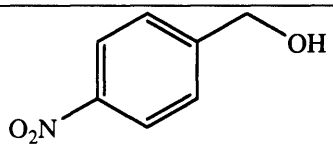
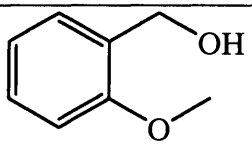
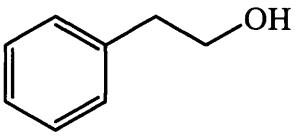
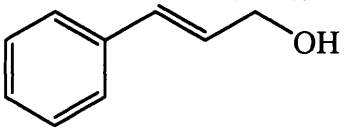
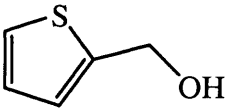
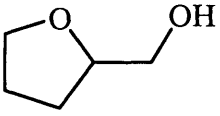
In order to examine if the oxidation with NMO as stoichiometric oxidant could be improved, a solvent screen was carried out using **111** (5 mol%), NMO (1.2 eq), molecular sieves (500 mg/mmol, finely ground) and tolyl alcohol (0.2M solution in solvent) as substrate, at room temperature for 24 hours. The catalyst was first added to the reaction solvent and sieves, followed by the substrate and finally NMO. Benzyl alcohol was selected as an appropriate substrate.

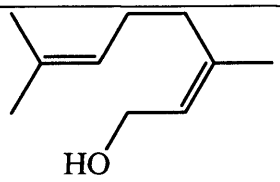
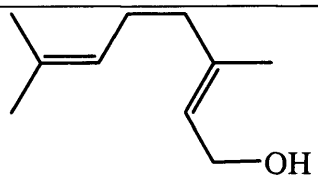
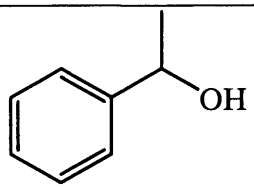
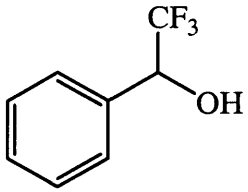
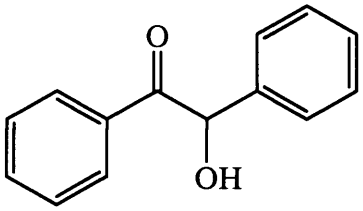
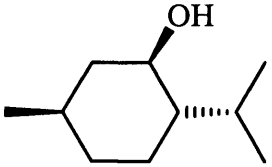
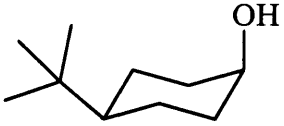
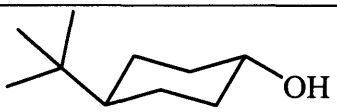
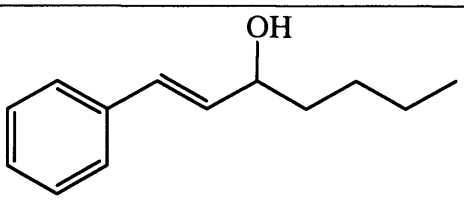
Solvent	Catalyst solubility	Yield (%)
Toluene	Fully	96
DCM	Fully	89
THF	Fully	84
Acetone	Forms red suspension	82
Pet. Spirits	Insoluble	75
Diethyl ether	Partial	68
DMF	Fully	67
Dimethoxyethane	Partial	45
Dichloroethane	Partial	39
Acetonitrile	Fully	23
MeOH	Fully	14
DMSO	Fully	2

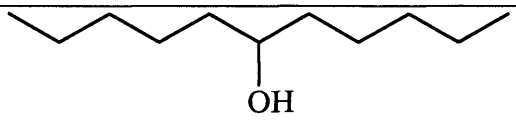
Table 15

The results in Table 15 show that aprotic, non-nucleophilic solvents offer the best yields. Even though the catalyst itself appeared to be insoluble in petroleum spirit, a very good yield of aldehyde was isolated, presumably due to the substrate increasing the solubility of the catalyst in the final reaction solution. We can also infer that nucleophilic, strongly coordinating, polar solvents limit the reaction. DCM was selected as the solvent for our reactions, as a consequence of its good performance in the solvent screen, its hydrophobic nature, and the low boiling point. The work up for these reactions involved simple filtration, removal of volatiles, and column chromatography to yield the pure product. Toluene, even though giving the best yield, was not selected as the solvent for the reaction as the loss of low boiling substrates or products could occur during solvent removal. A range of alcohols (Table 16) were then subjected to the optimal conditions *viz*: substrate (0.2 M in DCM), **111** (5 mol%), NMO (1.2 eq), molecular sieves (500 mg/mmol, finely ground), under a nitrogen atmosphere, for 24 hours at room temperature (*General method for the oxidation of alcohols promoted by NMO*). The quoted yield in Table 16 is an average of at least two runs.

Table 16

	Substrate	Yield (%)	TON
236		84	17
237		100	20
238		85	17
239		89	18
240		92	18
241		100	20
242		76	15
243		1	N/A
244		86	17
245		100	20
246		1	N/A

247		25	5
234		92	18
248		92	18
235		80	16
249		45	9
250		100	20
251		45	9
201		43	9
202		88	18
252		72	14

253		50	10

5.2.2 Interpretation of the results observed during the development of methodology for the N-oxide promoted oxidation of alcohols

The greater success of our catalyst for oxidation in non-coordinating solvents, as established by the solvent screen, Table 15, is easily understood. A strongly coordinating solvent will prevent the reaction proceeding by blocking the substrate from reaching the metal centre *via* competitive coordination, or indeed deactivate the catalyst either by displacement of a chloride or by preventing formation of the Ru-hydride species.

Although Sharpless[344] postulated that the initial step of the oxidation mechanism of alcohols using N-oxides was attack of the ruthenium complex by an alcohol to form an intermediate ruthenium hydride, which itself was oxidised to the ruthenium-oxo species be a molecule of NMO, we believe, based on the understanding we developed of these complexes during transfer hydrogenation experimentation, that the mechanism of Ru/N-oxide oxidation is more likely to proceed as outlined in Figure 69, with NMO forming the oxo species **255** from the dichloro species *via* an intermediate such as **254.** For clarity, the mechanism is drawn omitting the CNC pincer system, which is indicated only in the first structure.

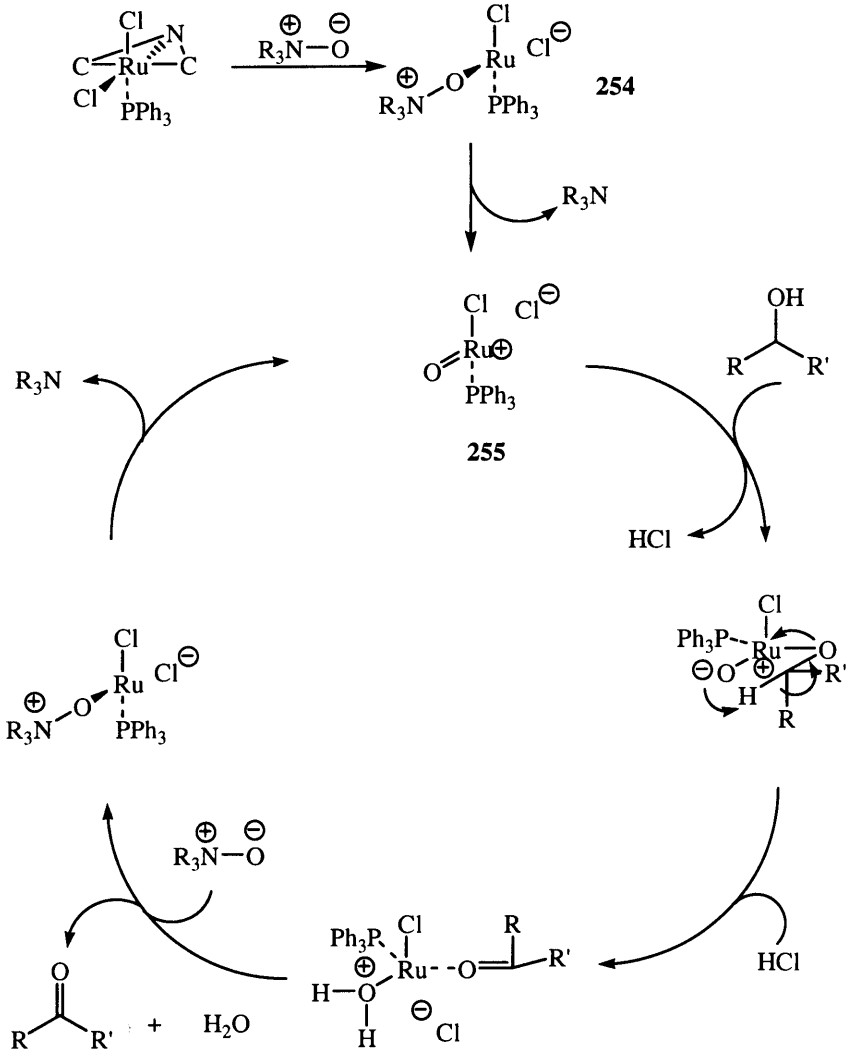


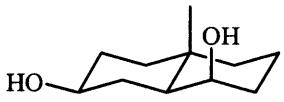
Figure 69

It is clear from this postulated mechanism that any coordinating solvents would very readily associate to the metal centre once it becomes electronically deficient after oxidation by NMO to the oxo species, **255**. The coordination of solvent molecules at this point in the reaction mechanism would limit the access of the substrate to the active catalytic site, as would the coordination of the tertiary amine released into solution after reduction of the N-oxide.

In chapter 1 we established that primary alcohols are more difficult to oxidise than secondary alcohols as the CH bond is stronger in the former compared to the latter. This can in part be overcome by activating the CH bond as is the case with primary benzylic alcohols or alcohols which are remotely activated i.e. *via* conjugation to an aromatic system, even the presence of a double bond such as in an allylic alcohol results

in sufficient activation to allow for much improved yields and the effect of such activation can be seen in the oxidation of substrates such as **236** – **245**, **234**, **248** and **250**. Electron rich (**238**) and poor systems (**241**) are equally well tolerated by the conditions employing NMO as co-oxidant, as are functionalities such as halides (**239**, **240**), and heteroaromatic rings (**245**). Steric encumbrance around the alcohol is also exceedingly well tolerated (**242**, **251**). The lack of reactivity of tetrahydrofurfuryl alcohol (**246**) under conditions where even decan-1-ol **247** is oxidised to a significant extent is somewhat surprising, but may imply that the oxygen atom of the furan ring is a competitive donor ligand. Acyclic α,β-unsaturated primary alcohols possessing defined geometry double bonds (**234**, **248**) are successfully oxidised, without any loss of geometric integrity. The lower yield of 2,2,2-trifluoro-1-phenylacetophenone **249** in comparison to acetophenone **235** is most likely attributable to the reluctance of the molecule to adopt sp^2 type hybridization, rather than simply due to it being an electron deficient alcohol. Secondary activated (**235**, **250**, **252**) and non-activated alcohols (**201**, **202** and **251**), as well as acyclic alcohols (**253**) are all successfully oxidised in good - moderate yields under these conditions (*General method for the oxidation of alcohols promoted by NMO*).

In the 1940's and 50's a lot work to understand oxidation mechanisms was underway, with particular interest in the search for reasons to explain the selectivity of oxidations.

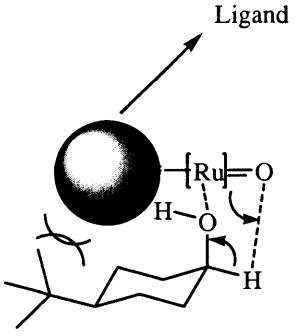


256

Figure 70

Eschenmoser and Westheimer published a series of papers demonstrating the effect that steric strain has on the decomposition of chromate esters, such as those formed during oxidation of alcohols, using reagents such as chromium trioxide.[346] Their observations were able to explain why in molecules such as **256**, the hindered axial alcohol is oxidised in preference to the exposed equatorial alcohol. If oxidation using the ruthenium complexes we prepared, proceeds *via* a ruthenium oxo species as detailed in the mechanism in Figure 69, bearing in mind the work of Eschenmoser and Westheimer

we might expect that the oxidation of *cis* 4-*tert*-butylcyclohexanol **201**, would occur faster than that of the *trans* alcohol, even though the effect of a 1,4 steric interaction is much less than a 1,3 interaction. A 1,4 interaction could be expected between the ruthenium complex approaching the alcohol on the same face as that of the protruding *tert*-butyl group as depicted in Figure 71, accelerating decomposition of the Ru-ester to give the ketone in order to release the strain.



257

Figure 71

However this is not the observed result. If the mechanism in Figure 69 is correct, then the hydroxyl group of the alcohol must approach the ruthenium centre in a similar manner to that of **257** above. The necessity of this 5-membered transition state in order for the reaction to proceed results in a limited number of conformations that the alcohol can make with the ruthenium complex. One of these is as presented C in Figure 72, but this particular representation is unlikely to occur, as the cyclohexane ring with its bulky *tert*-butyl group is required to assume a position close beneath the plane of the ligand. More likely are conformers A and B, Figure 72.

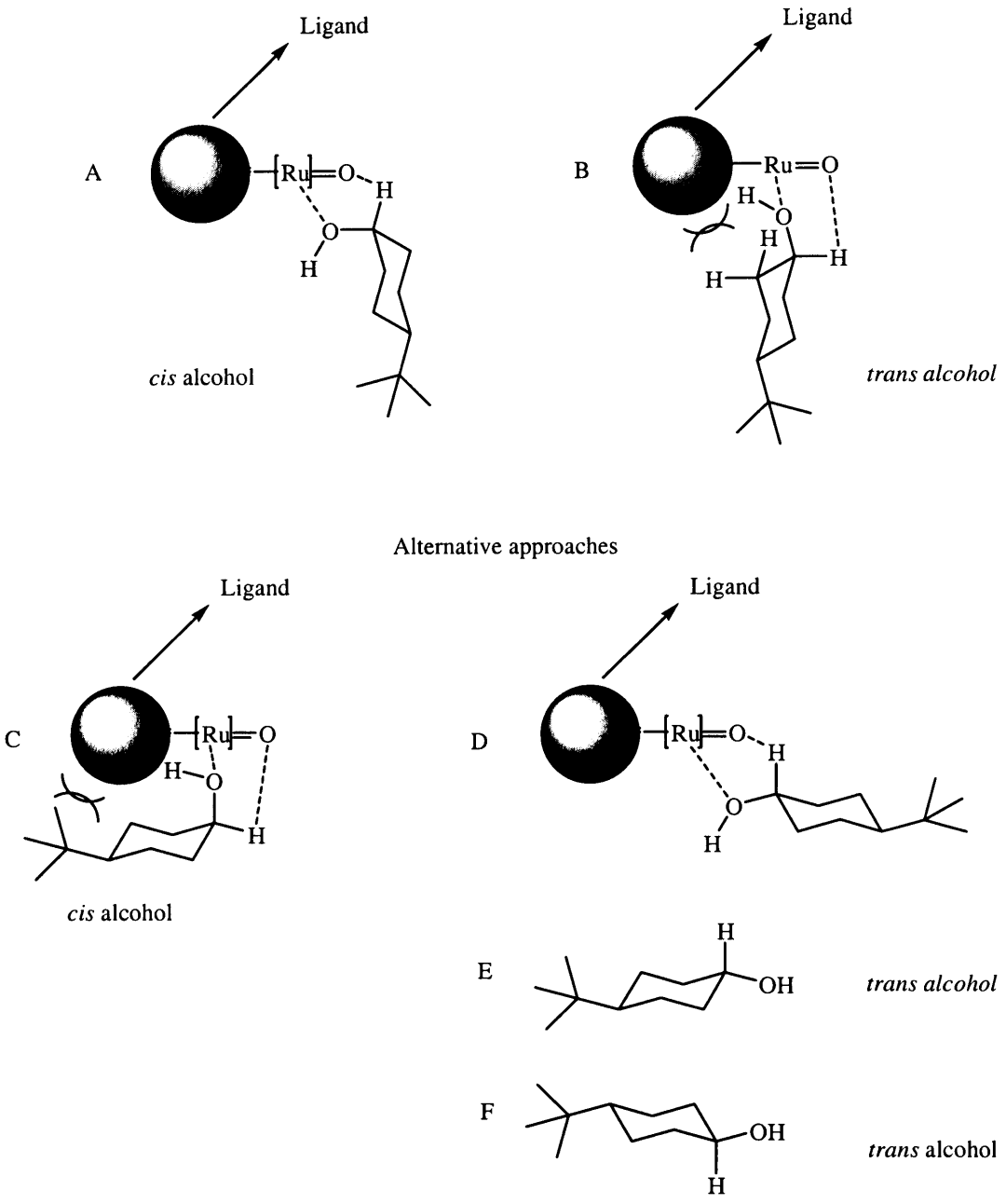


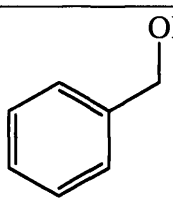
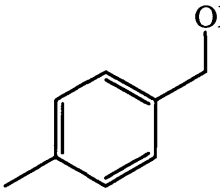
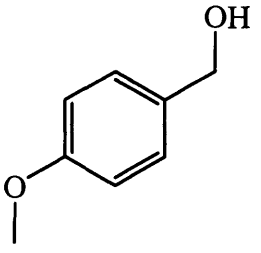
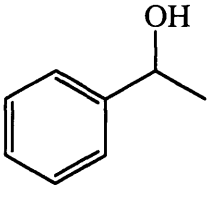
Figure 72

Under these geometric constraints the *cis* alcohol **201** finds itself in an accommodating 5-memberd ring (position A), with minimal steric interaction and so the reversibility of the Ru-ester becomes the rate-limiting step. The associated reduced rate of product formation with reversible Ru-ester formation gives molecules of reduced N-oxide the opportunity to poison the catalyst. In the case of the *trans* alcohol **202**, adoption of a similar 5-membered transition state to **201** induces a degree of steric interaction between the protons of the CH_2 group adjacent to the hydroxyl group and the ligand. This may be sufficient to promote an accelerated decomposition of the ruthenium ester,

analogous to that observed for chromium oxidations. Other possible conformations, D, E, and F offer poorer interaction between the substrate and complex.

5.2.3 Trimethylamine-N-oxide

We held a suspicion that the reduced form of NMO, *N*-methylmorpholine could be responsible for the long reaction times of our oxidations by poisoning our catalyst *via* equatorial chloride displacement (*cf.* **114**). In order to overcome this possibility, we therefore investigated the use of trimethylamine-N-oxide (TMANO) as the stoichiometric oxidant, since the reduced product, trimethylamine, is volatile (BP 3°C[347]) and we hoped that, by passing a stream of nitrogen through the reaction solution, we would be able to drive off this volatile amine before it had an opportunity to poison the complex. Substituting TMANO for NMO, we then compared the relative yields for a selection of substrates (*General method for the oxidation of alcohols promoted by TMANO*). The quoted yield in Table 17 is an average of a minimum of two runs.

	Substrate	NMO Yield (%)	TMANO Yield (%)
236		84	69
237		100	86
238		85	86
235		80	71

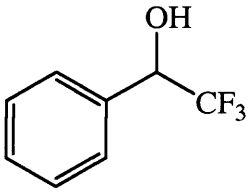
249		45	29

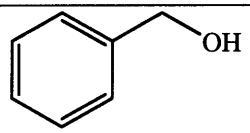
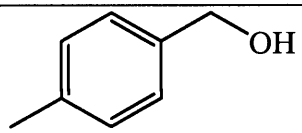
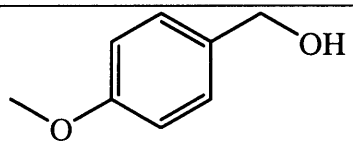
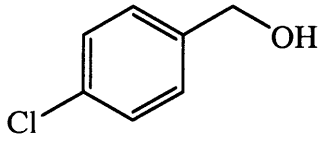
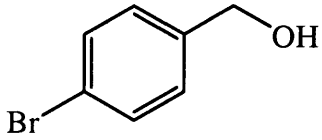
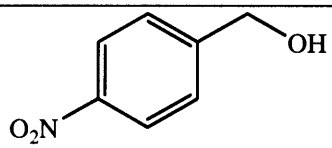
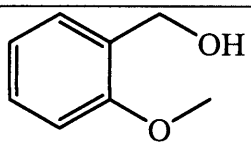
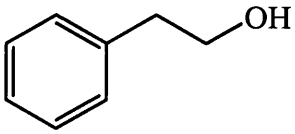
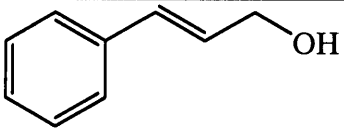
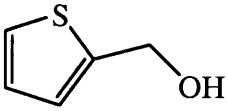
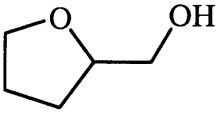
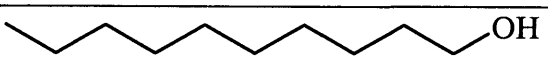
Table 17

Table 17 demonstrates that the results using TMANO are consistently lower than those achieved with NMO, possibly due to the fact that although trimethylamine is volatile, it is also less hindered and more nucleophilic than *N*-methylmorpholine.

The mechanism of TMANO mediated oxidations is the same, but the poisoning of the complex is more efficient due to the enhanced nucleophilicity,[348] and smaller size of the resulting amine.

5.2.4 *Tert*-butylperoxide

Peroxides are well known oxidants[349] and have been coupled with ruthenium-based catalysts for oxidation previously.[350] *Tert*-butyl peroxide in particular has many advantages in comparison to other peroxides, possessing good thermal stability ($t_{½}$ ~520 hours at 130°C for a 0.2 M solution in C_6H_6), not very corrosive, and very soluble in non-polar solvents. Also the reduced product (*tert*-butanol) is easy to separate by distillation and can be recycled or used for other industrial processes should the reaction be run on an industrial scale. It is also much safer to prepare non-aqueous solutions suitable for sensitive chemistry unlike H_2O_2, whose reduced product in any event is water.[351] Using *tert*-butylperoxide as an oxidant in conjunction with our ruthenium complex offers a further key advantage - there is no side product to poison the complex as was the case for the amine oxides. Several experiments were therefore carried out to develop satisfactory conditions for oxidation in DCM using **111** (5 mol%), whilst maintaining the 0.2M substrate concentration, 24 hour reaction time and room temperature conditions as used for the N-oxides, but this time using *tert*-butylperoxide as the stoichiometric oxidant. The order of addition of reagents proved to be critical. If the peroxide (1.0 eq) was added to a solution of catalyst before substrate addition (*p*-tolyl alcohol), rapid reduction of the oxidant occurred, resulting in poor yields of product (*p* -tolualdehyde, 33%). However, if the peroxide was added to a solution of the catalyst and substrate, a better yield was isolated (*p*-tolyl alcohol, 45%). It was found that oxidation of the substrate using peroxides as stoichiometric oxidants occurs at a much faster rate than that seen with N-oxides, with a yield of 45% being reached in only 2 hours. Extending the reaction time, or increasing the reaction temperature to 40 °C, offered no benefits. Slow addition of 4 equivalents of peroxide over 2 hours, with stirring for a further 2 hours resulted in the best results for a range of compounds (*General method for the oxidation of alcohols promoted by tert-butylperoxide*). The results are summarised in Table 18 and are an average of a minimum of 2 runs.

	Substrate	Yield (%)	TON
236		8	2
237		52	10
238		52	10
239		24	5
240		46	9
241		52	10
242		30	6
243		0	N/A
244		47	9
245		31	6
246		0	N/A
247		0	5

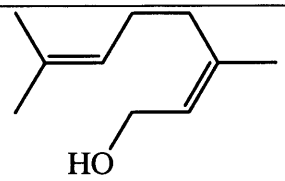
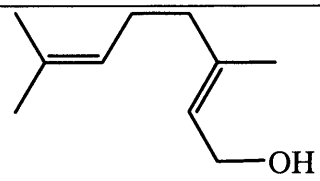
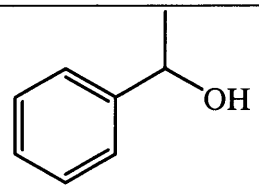
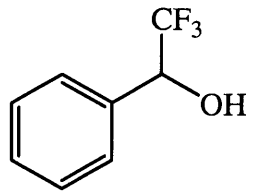
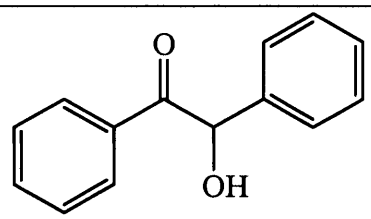
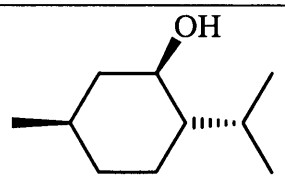
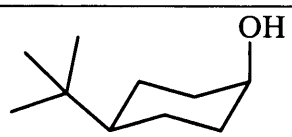
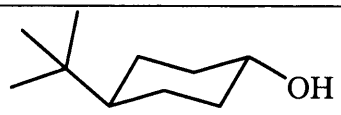
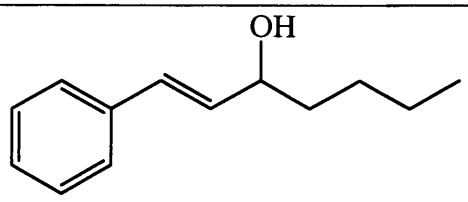
234		51	10
248		38	8
235		12	2
249		0	N/A
250		29	6
251		0	N/A
201		18	4
202		8	2
252		40	8

Table 18

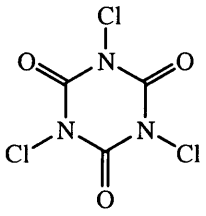
The results in Table 18 are consistently lower than those achieved by NMO and the reaction is much more sensitive to the substrate.

5.2.5 Interpretation of the results observed during the development of methodology for the *Tert*-butylperoxide promoted oxidation promoted oxidation of alcohols

The results of peroxide mediated oxidations (Table 18) essentially mirror the selectivities observed with the N-oxide based oxidations (Table 16 and Table 17). Activated primary (**234**, **237** – **242**, **244**, **245** and **248**) and secondary (**235**, **250** and **252**) alcohols are oxidised, albeit in lower yields than the N-oxide version of the methodology. Unactivated substrates, primary (**213**, **246** – **247**) or secondary (**201**, **202** and **251**) are generally unreactive under peroxide conditions. It is possible that there is competition between the transition metal promoted disproportionation of the peroxide to *tert*-butanol and oxygen (kinetically favoured), and the reoxidation of the ruthenium to the desired oxo species **255**. We believe this to be the case for several reasons. Addition of the peroxide to a solution of **111** or **112** results in rapid effervescence, and if the substrate is then added, there is minimal oxidation. If this order of addition is reversed, oxidation occurs in much improved yields. Should the peroxide be added slowly, the yield of oxidation increases further. These results are consistent with decomposition of our oxidising agent by the metal complexes. When the results in Table 18 are studied, it becomes apparent that substrates with increasing steric bulk, which, presumably take longer to associate to the metal, give lower yields e.g. 4-methoxy- **238** *vs.* 2-methoxybenzyl alcohol **242**. The case of nerol **248** *vs.* geraniol **234** is another example where increased steric encumbrance affects the yield. In general, substrates which proved difficult to oxidise with N-oxides were also unaffected by the peroxide method, due to the kinetically favoured consumption of the oxidant.

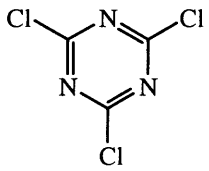
5.2.6 Trichloroisocyanuric acid

Trichloroisocyanuric acid **258** (TCCA) is a cheap, safe and efficient reagent useful for chlorination and oxidation, exhibiting good solubility in common organic solvents.[352] The structure of TCCA has commonly been confused with that of cyanuric acid **259**, to the point where in early editions of Fieser and Fieser it was incorrectly represented as such.



Trichloroisocyanuric acid

258

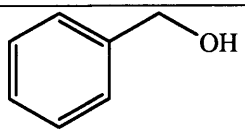
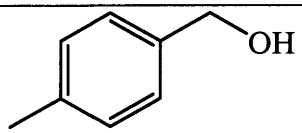
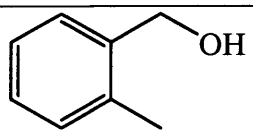
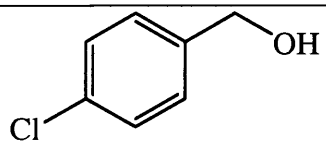
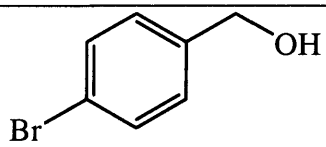
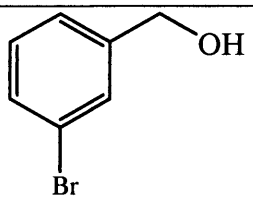
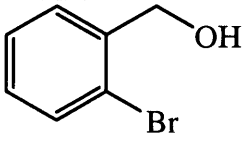
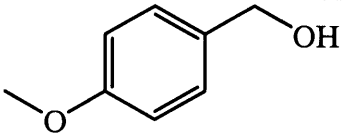
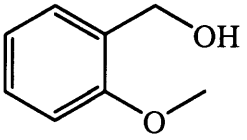
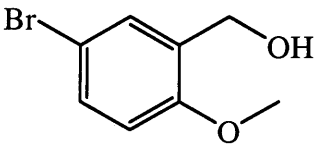


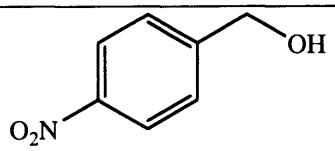
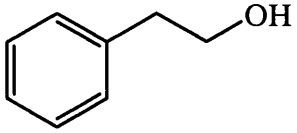
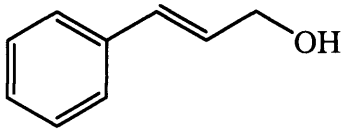
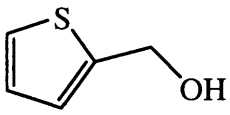
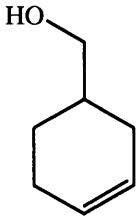
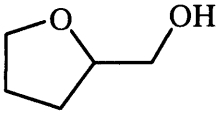
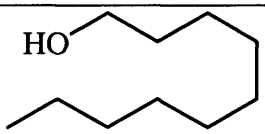
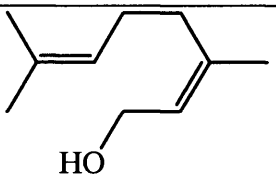
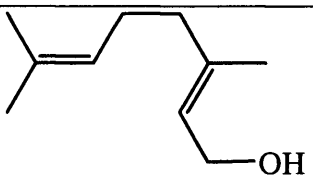
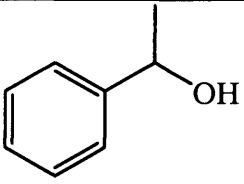
Cyanuric chloride

259

Figure 73

Many studies on the use of TCCA in conjunction with $RuCl_3$ for oxidation have been reported,[353] and this prompted us to investigate its use as a further method for oxidation of the Ru complexes. The reduced products of TCCA are the poorly nucleophilic cyanuric acid, and HCl, neither of which should affect the NHC complexes, especially as a base (K_2CO_3) is included in the reaction to neutralise the liberated acid. In particular we elected to examine the biphasic conditions of Ikunaka[353f] **111** (1 mol%), the phase transfer catalyst tetrabutylammonium bromide (4.0 mol%), K_2CO_3 (3.0 eq) and TCCA (0.7 eq) were added to the alcohol (0.3 M in EtOAc/Water 1:1 v/v) and stirred under ambient conditions for 1 hour (*General method for the oxidation of alcohols promoted by tert-butylperoxide*). The results are summarised below with the yields reported being the average yields from a minimum of two runs.

	Substrate	Alcohol (%)	Aldehyde (%)	Acid (%)
236		0	78	22
237		0	100	0
260		0	100	0
239		0	100	0
240		0	100	0
261		0	100	0
262		0	100	0
238		49	37	14
263		77	23	0
264		0	100	0

241		0	43	57
243		86	14	0
244		0	Decomp.	Decomp.
245		0	Decomp.	Decomp.
265		0	Decomp.	Decomp.
246		0	Decomp.	Decomp.
247		98	2	0
234		0	Decomp.	Decomp.
248		0	Decomp.	Decomp.
235		0	100	N/A

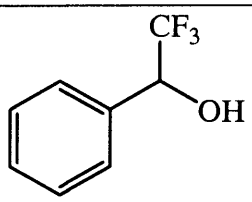
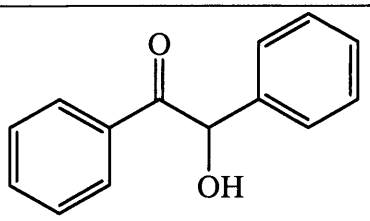
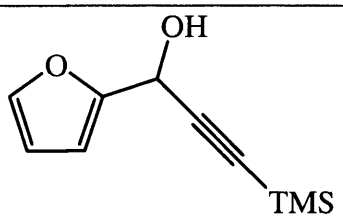
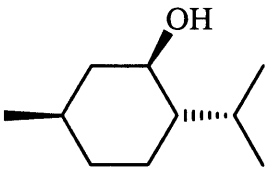
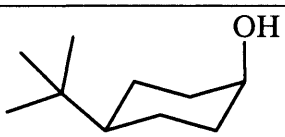
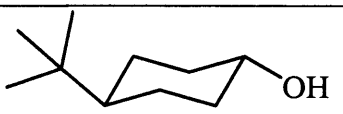
249		50	50	N/A
250		41	59	N/A
266		0	Decomp.	Decomp.
251		55	45	N/A
201		25	75	N/A
202		81	19	N/A

Table 19

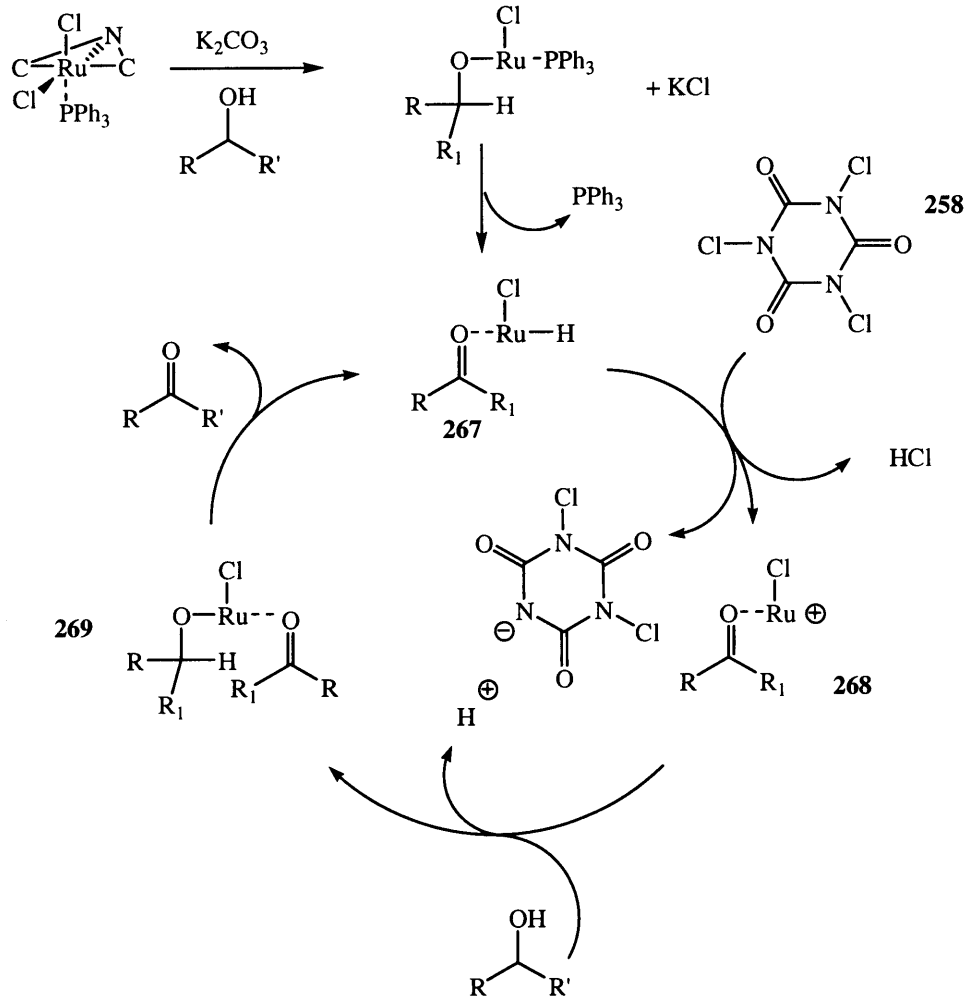
Decomp. in Table 19 indicates intractable product mixture/decomposition.

The results from Table 19 demonstrate this method to be active for a range of alcohols, but is at times unselective, resulting in over oxidation to the acid in some cases.

5.2.7 Interpretation of the results observed during the development of methodology for the Trichloroisocyanuric acid promoted oxidation promoted oxidation of alcohols

TCCA **258**, is a very efficient oxidising agent as only 1/3 of a molar equivalent is required for complete oxidation of a given substrate.[352]

The mechanism for oxidation begins with the reaction of an alcohol with a Ru-complex to give a ruthenium hydride **267** and a molecule of product (which may or may not act as a temporary ligand in place of the phosphine) in the by now, established manner. The Ru-H species can then transfer its hydride to a molecule of TCCA with subsequent formation of a molecule of HCl and the 17-electron ruthenium cation **268**, which is quickly neutralised by the substrate alcohol to form the stable 18-electron ruthenium alkoxide **269**. Disassociation of a ligand followed by a β-hydride elimination reaction can then reform the 18-electron species **267** and another molecule of product, Scheme 65.



Scheme 65

The most striking observation about TCCA mediated oxidations is its relative intolerance to functional groups. This is not wholly unexpected, as TCCA is a potent chlorinating agent, and has been shown to oxidise double bounds in a non-predictable manner.[353f] In our examples *any* molecule possessing points of unsaturation (other than aromaticity) or heteroatom substitution were completely consumed, with intractable mixtures of products being recovered e.g. **234**, **244**, **245**, **248**, **265**, and **266**. An interesting case was that of the silyl protected alkyne **266** from which the desilylated material was recovered in 35% yield. In addition, the first time in our oxidation studies we see over oxidation to acid, possibly as a consequence of operating under biphasic conditions under which an aldehyde may be hydrated and subsequently further oxidised. All simple benzylic compounds are oxidised in excellent yields, with a high degree of tolerance to steric encumbrance. The exception to this is the electron rich methoxy-substituted aryl rings **238** and **263**, which proceeded in low yield. This negative effect

of high electron density affecting the oxidation is confirmed to some extent by modulation of the effect through introducing a bromine atom in a *para* position to the donating methoxy substituent as in **264**, which results in a quantitative conversion to the aldehyde. Further oxidation to the acid is seen only in three examples, rings possessing strongly electron donating groups *para* to the alcohol (4-methoxy, **238**), strongly electron withdrawing rings groups *para* to the alcohol (4-nitro, **241**) and the 'electronically neutral', benzyl alcohol, **236**. It is common to observe however, auto-oxidation of benzaldehyde to benzoic acid,[354] and this may have occurred to a certain extent in this case. Literature shows that this particular oxidant (TCCA) is sensitive to the pH, temperature, solvent, and added base as to whether the product is oxidised to the acid or stops at the aldehyde, and so there may be several factors affecting the final product distribution.[353f] Primary unactivated alcohols are oxidised in low yields (e.g. **243**, **246** or **247**), as with other methods, for the reasons discussed previously Secondary alcohols (e.g. **235**, **249**, **251**) are oxidised in similar yields to the NMO methods. Interestingly in the oxidation of the *cis* (**201**) and *trans* (**202**) 4-*tert*-butyl cyclohexanols we see the reverse selectivity to that observed under the N-oxide promoted reaction is observed.

Chapter 6

Novel Ligand synthesis

6.1 ACAC mimics

Throughout our studies, an ongoing research theme was the search for novel *N*-heterocyclic carbene ligands, especially those which could be of wide use in a variety of different metal catalysed reactions.

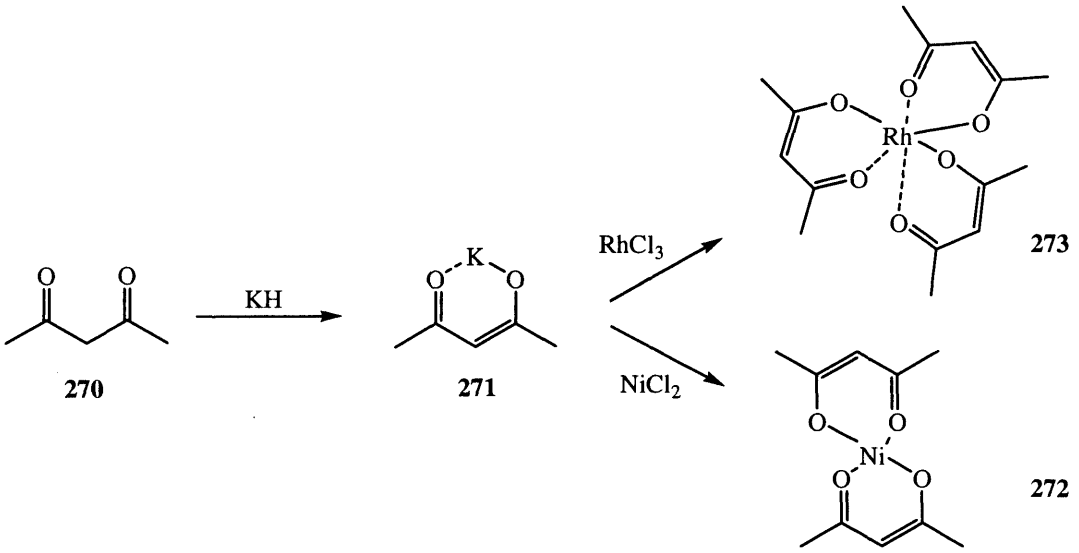
The acetylacetonate (acac) ligand, for example, is hugely popular and complexes with a vast range of metal care commercially available as demonstrated by the highlighted elements in Figure 74.[355] Complexes of many other metals such as Tc,[356] Ge,[357] W,[358] Os,[359] and Lu[360] have also been published.

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba		Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra		Rf	Db	Sg	Bh	Hs	Mt	Unn								

La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Figure 74

Deprotonation of pentan-2,4-dione **270** with a suitable base results in a bidentate, anionic chelating ligand which bonds to a metal *via* the alkoxide oxygen with further coordination through the carbonyl oxygen atom lone pair. This results in a very stable 6 membered chelate ring capable of supporting the metal. Different ratios of metal to acac ligand can occur, with 1:1 (e.g. **271**), 1:2 (e.g. **272**) and 1:3 (e.g. **273**) being the most common, Scheme 66.



Scheme 66

With these thoughts in mind, we therefore considered that it would be of interest to replace the carbonyl oxygen atom lone pair donor in acetylacetonate by the carbon atom of an *N*-heterocyclic carbene unit as depicted in Figure 75.

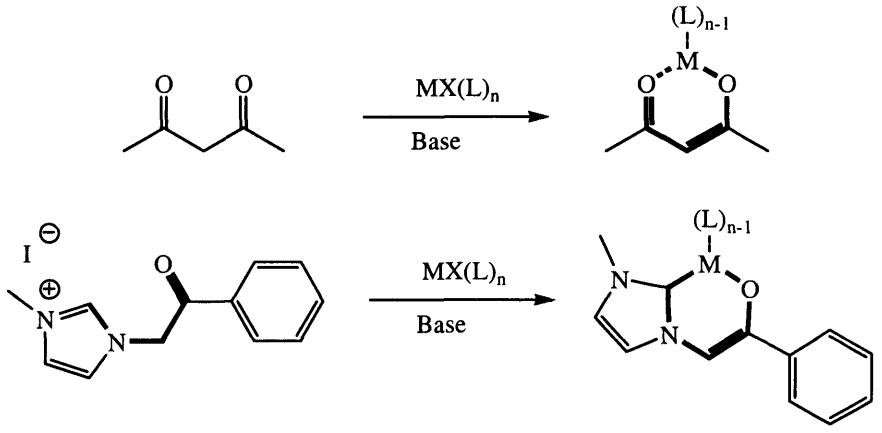


Figure 75

It was envisaged that the carbene unit could bring with it the advantages of tuneable electronics, stronger chelation to the metal, and simpler methods for control of the steric environment around the metal centre. The potential to alter the properties of the bonding alkoxide functionality *via* electronic and steric effects offers further possibilities to produce interesting complexes.

Bidentate or polydentate ligands that contain a mix of strong and weak donor groups have found widespread use in homogeneous catalysis. Use of the 2-pyridylphosphine-palladium complex **274** in the carbonylation of alkenes,[361] and the P-O chelating ligand **275** used in conjunction with Ni in the Shell higher olefins process (SHOP)[362] are examples of ligands containing a mixture of donor groups, one of which can be viewed as weak or hemi-labile, Figure 76. The hemi-labile arm in such ligands is capable of reversible dissociation from the metal centre, thus exposing a vacant coordination site, allowing complexation of substrates during the catalytic cycle, whilst the strongly donating moiety remains bonded to the metal centre, supporting it during the catalytic cycle, and therefore offering a catalyst with high TON's, and TOF's.

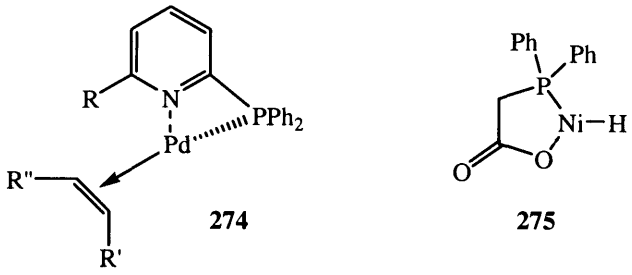
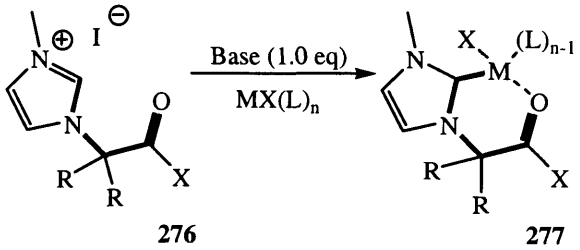


Figure 76

A further possibility within the framework is shown in Figure 77, whereby, if enolisation of the carbonyl unit is blocked (e.g. **276**), the carbonyl group can also function as a hemilabile ligand in such systems (e.g. **277**).

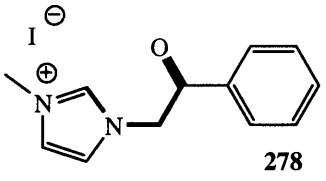


R = alkyl
X = Ar, NR_2, etc

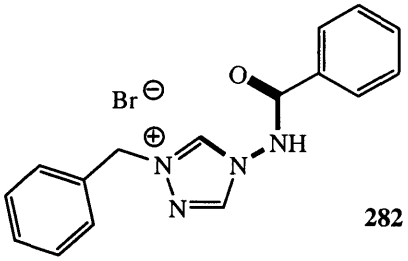
Figure 77

6.1.1 Complex synthesis

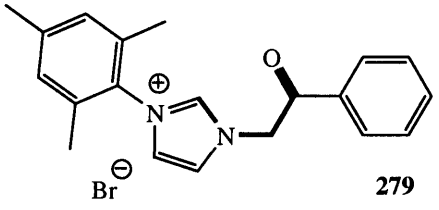
The initial acac mimics synthesised were the two very simple analogues **278** and **279**. These were designed to replicate acac as closely as possible, directly substituting the carbonyl unit for a simple alkyl/aryl substituted carbene. The enolisable functionality present in acac is represented in these two ligands as the acetophenone based moiety. Further alteration of these basic acac mimics can then allow us to replace the simple enolisable ketone with amide **280**, hydrazide **281**, **282** and urea **283** functionalisation. This series will allow us to study the effect of the different degrees of electron density on the metal centre provided by the various functional groups employed (Table 20).



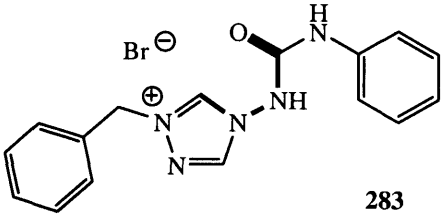
278



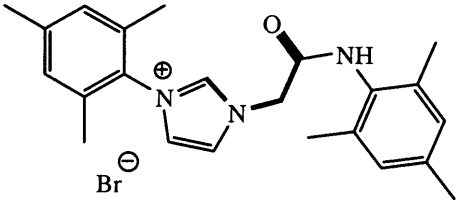
282



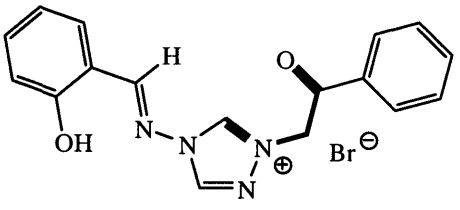
279



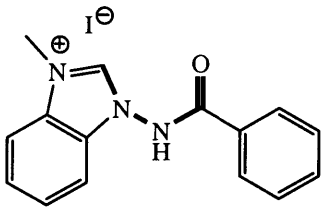
283



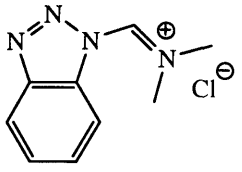
280



284



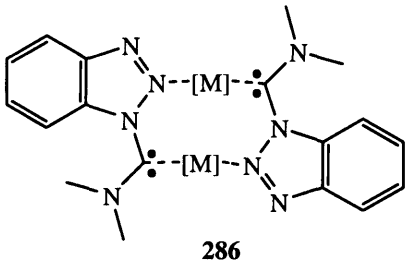
281



285

Table 20

An effective method to alter the extent of electronic donation to the metal from the carbene is alteration of the aromatic core, which supports the ligand.[363] These different scaffolds, especially benzimidazole, can have the additional effect of making the free carbene more stable, and thus potentially allowing isolation the free carbene species. An additional level of interaction between ligand and metal is possible for the salicaldehyde based triazole **284**. It is not unusual for several acac ligands to bind to a single metal centre and the hydroxyl functionality may result in a further type of interesting chelation method. A further ligand in Table 20 is **285**,[364] with the unusual feature of having an exocyclic carbene, which could potentially lead to novel ligand-metal complexes such as that postulated in Figure 78. All ligands in Table 20 were synthesised following the corresponding methods detailed in the experimental section of the present thesis.

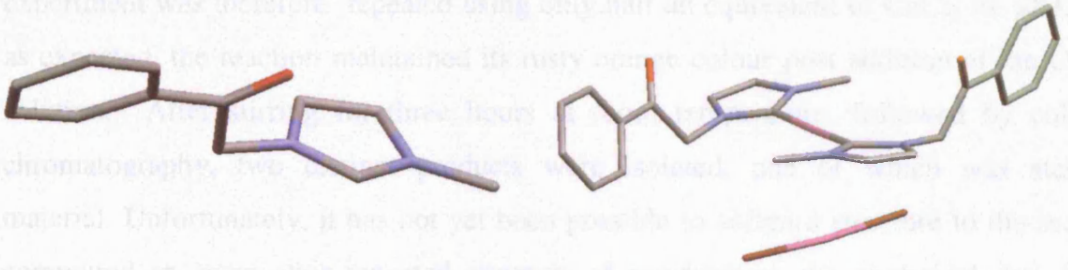


286

Figure 78

Initial deprotonation attempts of each ligand from Table 20 using KHMDS (1.0 or 2.0 eq) in THF at –78 °C, following procedures that were successful for compounds such as **111** and **112**, resulted in decomposition products being recovered. In order to investigate which is the most acidic site in each molecule, the C_1-carbene proton or the α-carbonyl proton, we attempted deprotonation, using KHMDS again in THF at –78 °C, but rather than attempting to isolate the species, the reaction was quenched with MeOD in anticipation of recovering the deutero labelled compound. This process was attempted at -78°C, -50°C, -35°C and 0°C, however, in every case complete degradation of the substrate molecule was observed, leading us to believe that these compounds are unstable once an anion is formed. This prompted us to investigate alternative methods for synthesising a metal complex, and as the substrates are sensitive to basic conditions, *in-situ* formation using one of the many methods available for the conversion of imidazolium based salts to transition metal complexes appeared to be an attractive

option. We first investigated a variety of conditions for the formation of palladium complexes of the ligand precursors in Table 20. Treatment of each ligand **278** – **285** (1.0 – 3.0 eq) with $Pd(OAc)_2$ in THF,[365] either at room temperature or at reflux, with or without additives such as NaI and KO^{t}Bu,[366] or DMSO,[367] was unsuccessful in forming the carbene complex. Reaction of $Pd(OAc)_2$ in a solution of DMSO and ligand precursor[368] resulted either in recovery of starting material or decomposition. The reactions in THF of **278** and **279** produced vividly coloured reaction solutions, yellow and orange respectively, but isolation of a complex was never achieved. Further attempts using $Pd(OAc)_2$ in dimethyacetamide (DMAC) with excess Na(OAc) as base were made at room temperature or reflux (120°C), without isolation of the Pd complex. Replacing the metal source with $PdCl_2(PPh_3)_2$ or $Pd(PPh_3)_4$ resulted in similar results in the case of each ligand. Treatment of the salts with silver oxide[369] in DCM or DCE at room temperature, or at the reflux temperature of the respective solvent overnight resulted in decomposition. The same experiments were repeated using silver carbonate,[370] but again, there was no evidence for the formation of the desired product. Phase transfer conditions[369] (NaOH/DCM, AgBr), were also unsuccessful. Other workers pursuing research into the area of functionalised carbenes have also made unsuccessful attempts to produce the free carbene or direct complexation of functionalised imidazolium salts with transition metals.[371] Finally however, treatment of **278** in DCM with silver oxide (2.0 eq) at room temperature for 2 hours yielded the silver complex, **286**. The X-ray structure of this complex and the starting imidazole **278** are shown in Figure 79.



278 **286**

Figure 79

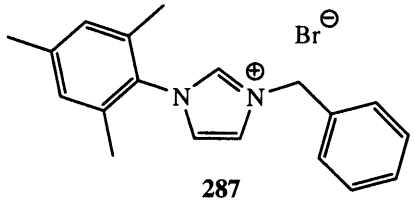
The X-ray studies reveal that the conformation adopted by **278** aligns the carbonyl groups away from the silver atoms, although in the starting imidazole, the carbonyl groups are in alignment with where the silver atom will be located. The silver complex, **286**, contains an Ag (I) cation supported by two NHC ligands and an $Ag(I)Br_2$ anion coordinating with it. Treatment of **286** with KHMDS (1.0 eq) in THF at –78 °C, -30 °C or at room temperature, with the aim of generating the enolate, resulted in decomposition. **278** is the only ligand from Table 20 where we had success in producing the silver carbene.

Attempts to produce a copper carbene, by a deprotonation, metal trapping technique, as used to prepare copper acac on an industrial scale were then made. When the effect of deprotonation, using KHMDS (2.0 eq) in THF, and trapping the intermediate with $CuCl_2$ (1.0 eq) was investigated with ligand **283** (1.0 eq) we observed an interesting result. Two equivalents of base were used in anticipation of simultaneously forming the carbene and deprotonating the amide. The reaction was performed at room temperature, allowing 15 minutes for deprotonation, observed by the initial white precipitate of triazolium salt **283** turning to a yellow/orange solution with a mild exotherm. The slow addition of $CuCl_2$ in THF to the reaction solution resulted however in a progressive darkening of the yellow/orange reaction solution. Removal of the volatiles after 3 hours stirring at room temperature resulted in an intractable mixture of products. It was noted during the experiment, that after addition of approximately half an equivalent of $CuCl_2$ to the reaction solution, the reaction still maintained its orange colour, which then disappeared to give the dark solution with further additions of the $CuCl_2$ solution. The experiment was therefore repeated using only half an equivalent of $CuCl_2$ *vs.* **283**, and as expected, the reaction maintained its rusty orange colour post addition of the $CuCl_2$ solution. After stirring for three hours at room temperature, followed by column chromatography, two distinct products were isolated, one of which was starting material. Unfortunately, it has not yet been possible to assign a structure to the second compound as, even after repeated attempts of purification, the analytical data is of insufficient quality and the interpretation of X-Ray data proved impossible, due to a high degree of disorder.

6.1.2 *In-Situ* catalyst formation

Given these unsuccessful efforts to isolate either the free carbene or a metal complex thereof, our thoughts then turned to an alternative approach. In many catalytic reactions where NHC's are employed as ancillary ligands, the corresponding imidazolium salts are used and deprotonated *in-situ*, avoiding the problems of synthesising and handling the air and moisture sensitive free carbene, or of isolating the complex. Thus, the first reaction to be investigated in this way was the Heck coupling of aryl halides with ethyl acrylate.

One further ligand **287**, which lacked the chelating carbonyl was prepared for comparative purposes. A further control employed during the following screening experiments was the inclusion of a blank reaction, which was set up in identical fashion to all others, but without a ligand precursor, in order to highlight any background reaction that may be occurring.



287

Figure 80

6.2 Heck coupling

6.2.1 Pd (0) Sources

Using conditions established in the literature[372] for the coupling of aryl halides with acyrlates using a Pd (0) source and an imidazolium salt, we screened the ligands in Table 20, for the Heck reaction, Figure 81.[373]

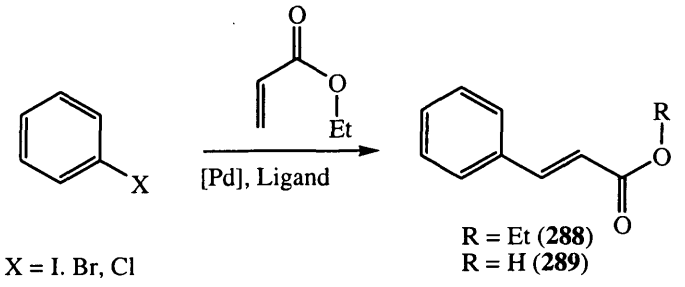


Figure 81

The conditions used were $Pd(dba)_2$ (1.0 mol%), imidazolium salt (1.0 mol%), Cs_2CO_3 (2.0 eq) added to DMAC, with stirring at room temperature for 30 minutes. Following this, a simultaneous addition of iodobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made, and the reaction mixture heated to 100°C (*Pd (0) catalysed Heck reaction – Method A)*). After 2 hours the blank reaction had led to quantitative coupling. Repeating the reaction at room temperature, but extending the time to 8 hours had the effect of reducing the yield for all ligands, whilst eliminating the blank reaction. The yield of coupled product in the reactions mediated by each ligand is detailed in Table 21.

Ligand	Yield of 288 at 100°C (%)	TON (TOF)	Yield of 288 at room temperature (%)	TON (TOF)
278	51	51 (26)	28	28 (4)
279	53	53 (27)	24	24 (3)
280	62	62 (31)	4	4 (0.5)

281	77	77 (39)	18	18 (2)
282	60	60 (30)	17	17 (2)
283	61	61 (31)	21	21 (3)
284	18	18 (9)	18	18 (2)
285	62	62 (31)	1	N/A
287	66	66 (33)	26	26 (3)
Blank	100	N/A	0	N/A

Table 21

In order to see if conditions which offered improved yields could be found, whilst keeping the background reaction to a minimum, bromobenzene was then selected as the aryl coupling partner. The reactions were slow at 100 °C, so the temperature was increased to 120 °C at which, after two hours, the reaction had stopped, and a palladium mirror was observed to have formed on the wall of the reaction vessel, to varying extents, depending on which ligand was used. The palladium mirror is, of course, indicative of complex degradation and metallic palladium deposition.

Ligand	**Yield of 288 at 120°C (%)**	**TON (TOF)**	**Extent of palladium mirror**
278	44	44 (22)	Significant
279	46	46 (23)	Significant
280	59	59 (30)	None
281	26	26 (13)	Significant
282	31	31 (16)	Small
283	36	36 (13)	Small
284	63	63 (32)	Significant
285	24	24 (12)	Trace
287	86	86 (43)	Small
Blank	19	N/A	Trace

Table 22

A further trial was conducted using chlorobenzene as the aryl partner for the coupling mediated by $Pd(dba)_2$. Using conditions identical to those for coupling bromobenzene, we observed no product. The only reactions that showed any effect were those containing amide/hydrazide ligands (**280**, **281**, **282**, and **283**) in which minute traces of palladium mirror were observed to occur.

A report in the literature recommended using dioxane as solvent.[374] The conditions we applied were very similar to those of *Pd (0) catalysed Heck reaction – Method A*. This set of conditions resulted in a side reaction not seen when using DMAC as solvent, in that a significant amount of the coupled product was recovered as the acid **289**, rather than the ethyl ester **288**. The results of these reactions presented in Table 23, are not as good as those seen using DMAC as solvent (Table 22) and this trend will be discussed further in section 6.2.3.

Ligand	Yield of 288 (%)	Ratio of 288:289	Total coupled Product (%)	TON	Extent of Pd mirror
278	14	1:0.38	19	13	small
279	12	1:0.46	18	12	small
280	14	1:0.37	19	13	small
281	9	1:0.79	16	11	trace
282	9	1:0.32	12	8	trace
283	10	1:0.37	14	9	trace
284	6	1:1.46	15	10	small
285	6	1:1.13	13	9	significant
287	10	1:1.23	22	15	small
Blank	1	1:0	1	1	trace

Table 23

Conditions: $Pd(dba)_2$ (1.5 mol%), imidazolium salt (1.5 mol%), Cs_2CO_3 (2.0 eq), dioxane, 30-minute stir, followed by addition of bromobenzene (1.0 eq) and ethylacrylate (1.5 eq) with heating at 80°C for 12 hours (*Pd (0) catalysed Heck reaction – Method B*)

A further Pd (0) source investigated for this set of conditions was $Pd(PPh_3)_4$, but with all ligands screened including the blank reaction, no product was detected.

6.2.2 Pd (II) sources

To complete the investigation of the suitability of our novel ligands towards the Heck reaction, several Pd (II) sources were studied. We used $Pd(OAc)_2$ as a Pd (II) source with conditions similar to those used in the literature,[375] ligand (2.5 mol%), $Pd(OAc)_2$ (2.5 mol%), Cs_2CO_3 (2.0 eq), dioxane or DMAC, 90°C overnight (*Pd (II) catalysed Heck reaction – Method A*). No palladium mirror was seen in the case of the Pd (II) catalysed reactions, with no acid detected, only ester or starting material being recovered.

Ligand	Yield of 288 (%) in Dioxane	TON	Yield of 288 (%) in DMAC	TON
278	8	3	42	17
279	6	2	46	18
280	6	2	29	12
281	12	5	33	13
282	8	3	30	12
283	9	4	31	12
284	6	2	28	11
285	9	4	36	14
287	11	4	40	16
Blank	2	N/A	6	N/A

Table 24

A second Pd (II) source trialled was $PdCl_2(PPh_3)_2$ with identical conditions as those applied for the $Pd(OAc)_2$ experiments, using dioxane (*Pd (II) catalysed Heck reaction – Method B*) or DMAC (*Pd (II) catalysed Heck reaction – Method C*) as the reaction solvent.

Ligand	Yield of 288 (%) in Dioxane	TON
278	54	3
279	60	2
280	3	2
281	19	5
282	29	3
283	35	4
284	27	2
285	11	4
287	42	4
Blank	28	N/A

Table 25

However, the blank reaction in DMAC gave a 37% yield of **288**, and due to this high background reaction, we decided to not explore the reactivity of the ligands in this solvent.

6.2.3 Interpretation of the results observed during the development of methodology for the Heck coupling reaction.

The results seen during the application of our range of ligands to the Heck reaction follow the expected trends of reactivity, i.e. I>Br>Cl. The use of Cs_2CO_3 as base is common due to its increased basicity and better solubility in organic solvents than K_2CO_3. It is not surprising for the blank reaction of aryl iodides with ethyl acrylate to produce coupled product, especially in chelating solvents such as NMP, DMAC, DMF or even TEA.[376] It is believed that the chelating solvent can support any colloidal palladium formed and hence catalyse the reaction. This may explain why, when the aryl iodide coupling reaction is performed at room temperature, with the associated reduced reaction rate, that the blank reaction produces no product but at elevated temperatures with increased reaction rates, product is recovered. Ligandless conditions developed by Jeffery involve the use of tetra-alkyl ammonium salts and solid bases in polar solvents with a typical reaction for the Heck type coupling of an aryl or alkenyl iodide using NH_4Cl and $KHCO_3$.[377]

The formation of a palladium mirror during our experiments is indicative of insufficient control of the catalytic cycle by the ligand and explains the low yields and poor rate. The stabilisation effect of a coordinating solvent on the palladium centre is not present when dioxane is used as solvent, and it is for this reason that we attribute the lower yields for the reaction when using this less strongly coordinating ligand *vs.* DMAC. The dioxane used in these reactions was dried before use, and so it is not apparent how hydrolysis of ester **288** is occurring, since the work up involved removal of volatiles *in vacuo*, followed by column chromatography in an identical manner to the reactions carried out in DMAC.

The failure of $Pd(PPh_3)_4$ to catalyse the reaction may offer us insight to one of the shortcomings of our methodology. The yields we have achieved although adequate are not good when one bears in mind the homeopathic levels[373] of palladium (0.0005 mol%) that can be used to affect a quantitative coupling between aryl bromides and styrene.[378] The problem associated with the use of $Pd(PPh_3)_4$ as the metal source is its over-ligation, impeding the coordination of substrates, and can even prevent more bulky

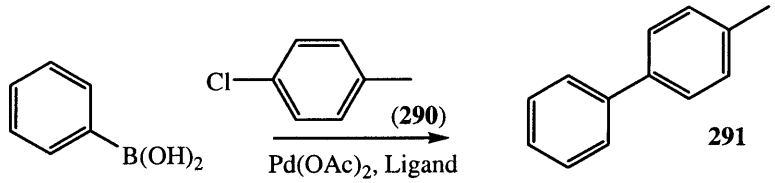
substrates from ever getting in proximity to the Pd-centre. We have seen from the X-ray diffraction study of the silver carbene complex 286, that two ligands have coordinated to the metal centre, and this could also be happening during *in-situ* palladium carbene complex synthesis. If this is the case, it may prove catastrophic to the reaction, as although phosphines coordinate effectively to the metal centre, their coordination is thought of as being reversible. One of the most striking physical properties of NHC based ligands however, is the incredible strength of the bond between them and the metal centre, meaning that their coordination is almost irreversible. The poor conversions may therefore be attributable to over-ligated palladium, hindering the substrates from coordinating.

With the application of our ligands to the Heck reaction using Pd (II) sources we found $PdCl_2(PPh_3)_2$ to be more reactive than $Pd(OAc)_2$. This enhanced reactivity may be a function of the ease with which the Pd (0) species is formed. Replacement of the phosphine ligands in the dichloropalladium species with NHC ligands may occur relatively fast, forming the electron rich, carbene supported intermediate. Oxidative insertion is accelerated for metals that have a high electronic density, and this may assist in a subsequent *in-situ* reduction of the Pd (II) species to the catalytically active Pd (0) species.

The ligand which consistently offered the highest yields of product was the simplest, unfunctionalised ligand that we synthesised **287**, which is incapable of acting as an acac type mimic, but rather can only act as a traditional carbene type ligand. This suggests that the activity observed during this reaction was most likely as a consequence of successful ligation to the Pd by a NHC ligand, in a traditional manner, rather than any beneficial effect of the chelation by the pendant carbonyl or enolate type unit.

6.3 Suzuki Coupling

We explored the suitability of our range of acac mimic ligands (Table 20) for Suzuki couplings using conditions from the literature for the *in-situ* formation of a palladium carbene suitable for this transformation.[379]



Scheme 67

The challenging substrate 4-chlorotoluene[380] **290** was chosen since the use of aryl chlorides as chemical feedstock's in coupling chemistry would be of considerable economic benefit in a number of industrial processes.[381] The conditions which gave the most successful results were 4-chlorotoluene (1.0 eq), phenylboronic acid (1.0 eq), $Pd(dba)_2$ (0.03 eq), ligand (0.03 eq), KOMe (3.0 eq), and TBAB (0.1 eq) in toluene at 40 °C, for 12 hours (*Pd (0) catalysed Suzuki reaction – Method A*). The use of TBAB is as a source of halide ions which stabilise the coordinatively unsaturated, low-valent palladium species.[382] Of all the ligands we tested, only **279** (28%) and **280** (35%) facilitated the reaction. The blank experiment produced no product.

6.3.1 Interpretation of the results observed during the development of methodology for the Suzuki reaction.

Previous work has shown that Suzuki–Miyaura coupling reactions can be achieved using Pd/imidazolium salt protocols.[383] These reactions have been typically carried out at temperatures between 70 – 80 °C and usually employ an excess of organoborane. We found our most successful ligands to be capable of facilitating the reaction at only 40 °C. There is only one other example of such mild conditions being used to couple challenging aryl chloride substrates, and in this case, using the same substrates, a yield of 75% was achieved in 24 hours[384] *vs.* 35% in 12 hours using our ligand, **280**. This paper highlights how sensitive the reaction is, as when 1,3-*bis*(*tert*-butyl)imidazolium chloride was used as the ligand precursor, no coupled product was detected, whilst the *bis*(2,6-di*iso*propylphenyl)imidazolium chloride precursor under identical conditions gave the best observed yield of 75% coupled product. Exchange of stoichiometric KOMe for catalytic amounts of KOMe and Na_2CO_3, a combination of bases which had been found to be optimum by other researchers,[385] resulted in 0% yield if the reaction using the optimum *bis*(2,6-di*iso*propylphenyl)imidazolium chloride ligand precursor was repeated.

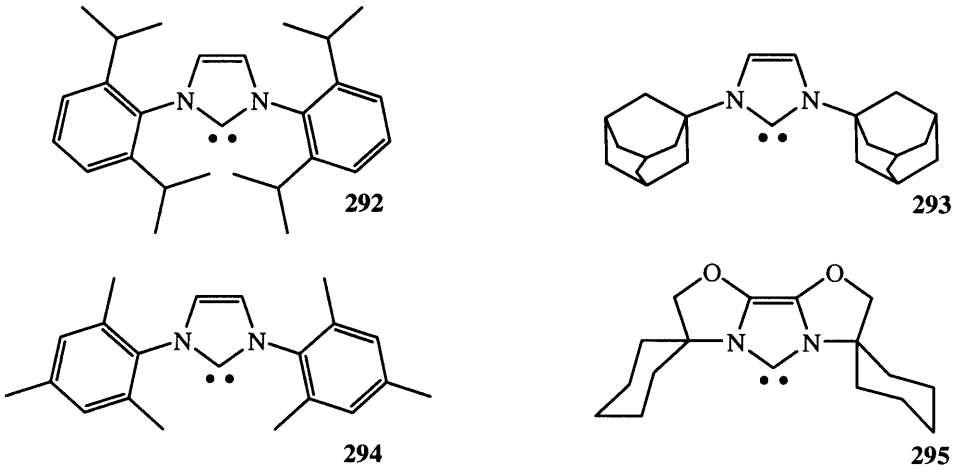


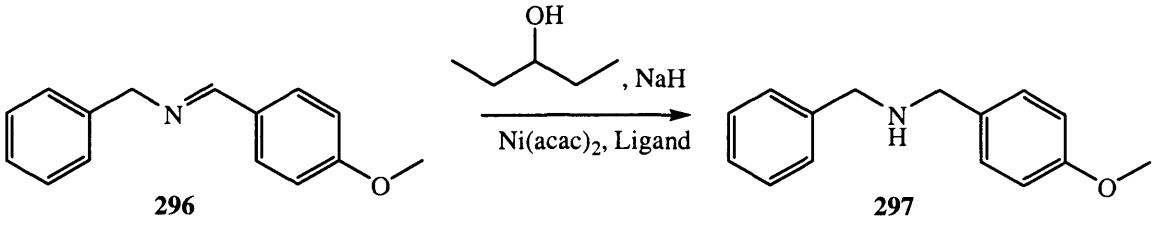
Figure 82

The most successful carbene ligands for the Suzuki reaction are featured in Figure 82.[386] The feature that each of these ligands has in common is the significant bulk they present to the palladium centre. Increased steric bulk promotes reductive elimination and is

believed to be responsible for the activity of these ligands. It is interesting to note therefore that of the ligands we synthesised, only the two ligands that contain the bulky mesityl substituent in conjunction with a nearby carbonyl unit (**279** and **280**), demonstrated activity for the Suzuki reaction. The simple unfunctionalised mesityl ligand **287** was unreactive, as was the methyl substituted ligand **278**, from which we can infer that the carbonyl unit on the two successful ligands was increasing their reactivity on steric grounds, rather than electronic. We know from the X-Ray structure of the silver carbene **286**, that the carbonyl group does not coordinate to the metal, but can provide flexible steric bulk that aids reductive elimination, but is able to rotate out of the way during oxidative insertion, as seen with the cyclohexyl groups on the pentacyclic ligand **295** of Glorius.[387]

6.4 Transfer hydrogenation of imines

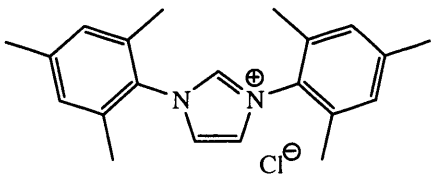
The reduction of C=N bonds is of great interest to the pharmaceutical industry as amines are present in many biologically active molecules. Reagents such as sodium borohydride or lithium aluminium hydride can be used in stoichiometric quantities to reduce ketones and imines, whilst sodium cyanoborohydride can selectively reduce an imine formed from a ketone and an amine in one-pot reductive amination procedures. Catalytic reduction is however preferred to stoichiometric reduction for large-scale industrial use, and both ketone[388] and imine[389] hydrogenation are well known. $Ni(acac)_2$ is commonly used for a wide range of transformations,[390] with transfer hydrogenation of imines being just one of the areas where this complex shows good activity and, as such, is an area where research of NHC supported Ni complexes could produce useful catalysts. The reduction of C=N bonds is more difficult than C=O, and hence comparatively few methods are available for their reduction, mostly utilising ruthenium or rhodium complexes.[391]



296 297

Scheme 68

The application of significantly cheaper nickel *vs.* ruthenium, rhodium or iridium has only, to the best of our knowledge, been used on two occasions for the transfer hydrogenation of imines. The first use of nickel in this way was when aluminium isopropoxide was combined with W-2 Raney nickel for the successful reduction of a range of imines. The authors demonstrated that this was not a MPV type reduction, and that the combination of Al and Ni complexes was key to the successful reduction.[392] The second occasion when Ni was demonstrated to facilitate transfer hydrogenation of imines was by Fort and co-workers,[393] who used simple imidazolium salts, the most successful of which are detailed in Figure 83, to form Ni-NHC complexes *in-situ*.



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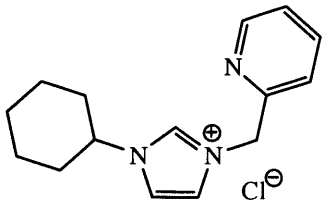


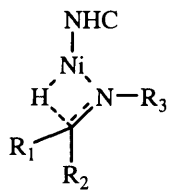
299

Figure 83

The *bis*mesityl (**298**) derived ligand reduced butyl-(1-phenylmethylidene) amine in 97% whilst the cyclohexyl (**299**) derived ligand achieved an 85% reduction of the same substrate, both after 3 hours at 100 °C in dioxane. Using our ligand range (10 mol%) in conjunction with the conditions of Fort ,[393] $Ni(acac)_2$ (10 mol%) in dioxane at 100 °C, with NaH (3.6 eq) and pentan-3-ol (3.6 eq) (*Ni catalysed transfer hydrogenation of imines – Method A*) as the 'hydrogen' source, we attempted the reduction of **296**. This substrate was chosen since the work by Fort *et al* showed that substrates with electron rich aryl rings were the most difficult to reduce. The blank reaction gave no product, and the only ligand that supported the reaction from our range was **283**, which resulted in a 31% yield of **297**, after 12 hours.

6.4.1 Interpretation of the results observed during the development of methodology for the reduction of imines.

The only previous example of NHC supported Ni facilitated transfer hydrogenation[393] revealed that increasing the electron density on the Ni centre reduces the activity of the catalyst. Substitution of **294** with the more electron-donating and bulkier **292** resulted in a dramatic decrease in activity from 97% reduction of N-benzylidenebutan-1-amine to only 4%. A further trend was found with bidentate type carbenes such as **299** in which the reduced steric demand of the system, compared to the *bis*adamantyl **293** or *bis*mesityl **294** substituted imidazoles, affords a greater activity for the reduction. For these reasons we would expect a ligand with minimal steric bulk and reduced electron donating capacity to be successful. Ligand **283** was the only successful compound from our ligand pool, with even the closely related amide analogue, **282** being inactive under the same conditions. Steric strain around the metal centre is kept to a minimum by use of a benzyl group in the case of **283** *vs.* direct aryl substitution (e.g. **279** or **280**), whist 1,2,4-triazoles are known to be less electron donating than imidazoles.[394] The combination of these factors is reflected in the activity of ligand **283**. The reasons for the failure of **282** are uncertain, but are perhaps due to the conformation which the molecule assumes, leading to a more hindered metal complex relative to the urea based ligand. The mechanism for the nickel promoted transfer hydrogenation of imines has not been fully elucidated, but is believed to proceed *via* a Ni-H species **291**, although an MPV-based mechanism **292** cannot be ruled out, Figure 84.[395]



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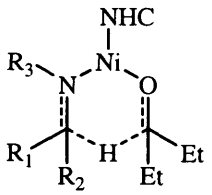
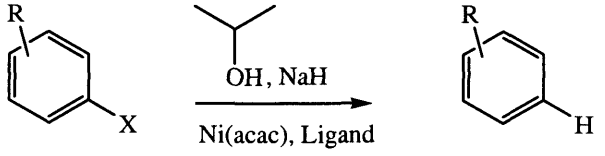


292

Figure 84

6.5 Dehalogenation of aromatic rings

Using nickel as the catalytic metal we attempted to dehalogenate 4-*tert*-butylchlorobenzene under conditions similar to those used for transfer hydrogenation. Dehalogenation of aryl rings is useful to organic synthesis, and is applied on an industrial scale,[396] with dechlorination of aromatic rings being of particular importance due to the negative environmental and health implications of chloroarenes.[397]



R = 4-*tert*butyl, X = Br (**293**) R = 4-*tert*butyl (**294**)

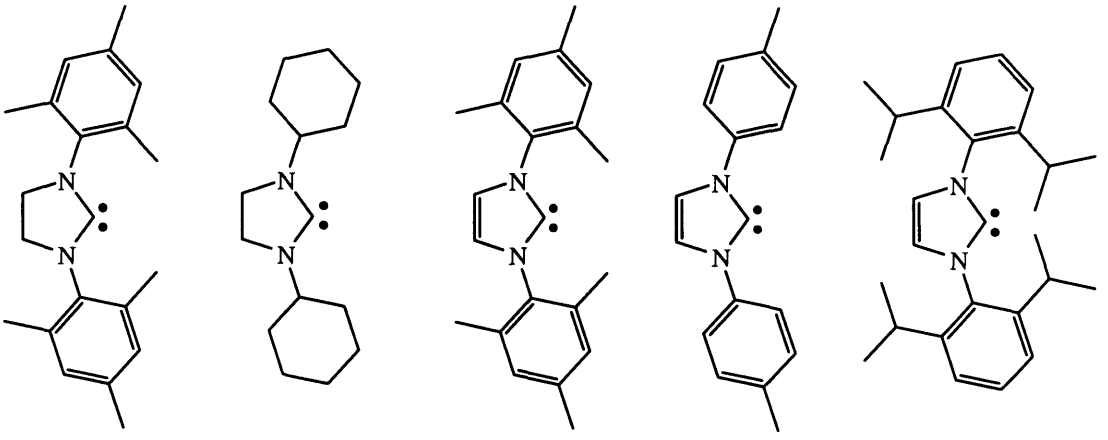
X = I, Br, Cl

Scheme 69

Clean reduction of aryl carbon-halogen to carbon-hydrogen conversion can be readily achieved by transition metal catalysed hydrogenation using palladium,[398] Pd/Fe-carbon composite[399] and nickel[400] catalysts, by reduction mediated by hydrides[401] or Grignard reagents.[402] $NiCl_2.H_2O$/Li/4,4'-di-*tert*-butylbiphenyl.[403] Raney Ni-Al alloy in alkaline solution,[404] or SmI_2/THF/HMPT[405] combinations have also been used for the successfully for the same purpose. Using nickel as the metal source poses obvious cost saving advantages over alternative metal sources such as palladium, and coupling nickel with a NHC ligand should hopefully reduce the amount of metal required, by offering a robust, active catalytic species. *In-situ* nickel carbene formation using **294** as the ligand precursor has been shown to be successful for this transformation.[406] Combination of $Ni(acac)_2$ (3 mol%), NaH (3.1 eq), ^{i}PrOH (3.0 eq) and ligand (6 mol%), in THF as solvent for the reduction of aryl chlorides (1.0 eq) (*Ni catalysed dehalogenation of aryl rings – Method A*) gave only 1 successful result. The reaction containing **279** as a ligand dehalogenated 4-*tert*-butylchlorobenzene in 13% yield after 12 hours, with further alteration of the number of ligand equivalents *vs.* metal having no beneficial effect. The blank reaction gave no dehalogenated product.

6.5.1 Interpretation of the results observed during the development of methodology for the dehalogenation of aryl halides.

Nolan has demonstrated that the Pd (0) complex of 1,3-*bis*(mesityl)imidazol-2-ylidene **295** and MeOK is effective for the dehalogenation of aryl chlorides and bromides in refluxing dioxane, but the Ni (II) salts, $Ni(OAc)_2$ and $NiCl_2$, investigated during his work as alternatives to palladium did not show any catalytic activity.[407] In the case of the palladium-mediated reaction, it was found that the success of the catalyst was critically dependant on the extent of electron donation to the metal centre. Use of the electronically rich, saturated NHC ligand **295** gave the best yield for the dechlorination of 4-chlorotoluene (96%), but increasing the electron density on the metal by using the bis cyclohexyl substituted ligand **296** gave only 2% yield. Reduction of the electron donating character of the ligand by application of the unsaturated *bis* mesityl species **297** resulted in only 46% dechlorination.



295 **296** **297** **298** **299**

Figure 85

In the case of the Ni catalysed reaction,[406] the critical factor appears to be the steric environment around the metal. Although there is a noticeable difference in yield between the saturated ligand **295** (55%) and unsaturated ligand **297** (96%) for the dechlorination of chlorobenzene, which is the reverse reactivity seen for the palladium catalysed reaction, the difference in reactivity as a function of steric mass is more significant. Application of the *bis*-tolyl **298**, *bis*-2,6-di*iso*propylphenyl **299**, and *bis*-

mesityl **297** imidazolidene as ligand results in yields of 32%, 59% and 96% respectively.[406]

The mechanism is proposed to proceed as outlined in Figure 86, with initial reduction of $Ni(acac)_2$ *via* a dihydride species leading to the NHC ligated Ni (0) intermediate **300**. Oxidative insertion of the aryl chloride to the electron rich metal centre gives a Ni (II) complex **301** that is attacked by an isopropoxide molecule to give **302**. A β-hydride elimination from the Ni-alkoxide produces an aryl-nickel-hydride **303**, which after reductive elimination reaction yields the product with concomitant reformation of the active catalyst, **300**.

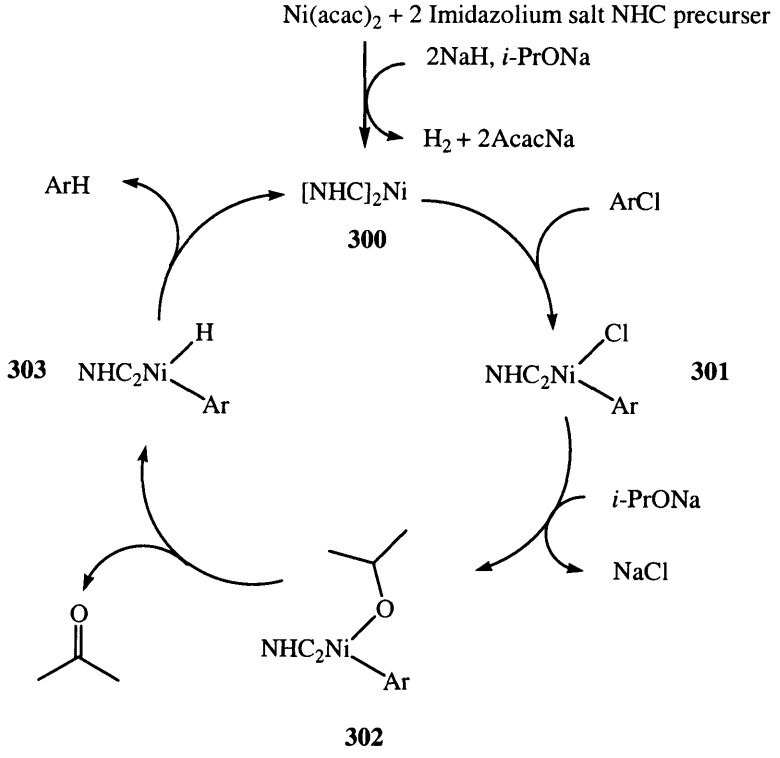


Figure 86

With an appreciation of this reaction mechanism and the trends that are observed in the literature, a ligand with moderate electron donating character and minimal steric hindrance would be expected to function well in this reaction. The electron donation of an aryl substituted imidazole, coupled with the relatively small steric footprint imparted by a fluxional carbonyl group as encompassed by ligand **279**, gave the best yield (13%) from the range of ligands in Table 20.

6.6 Kumada Coupling

The Kumada coupling falls into the C-C bond forming category of reactions, coupling an aryl halide with an organomagnesium fragment,[408] generally facilitated by palladium, Figure 87.

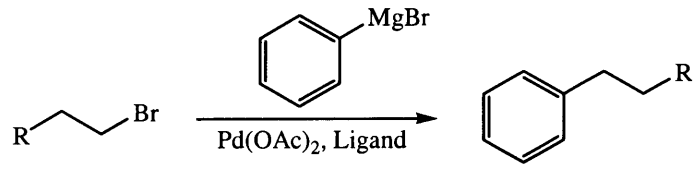


Figure 87

One of the main advantages of a Kumada coupling is its simplicity. Arylboronic acids used in the Suzuki coupling are commonly made *via* the Grignard reagent, and so a coupling reaction that uses the magnesium derivative directly, saves on performing this additional step.[409] One of the most challenging types of substrate to couple are alkyl halides due to the ease of β-hydride elimination from the palladium alkyl complex formed after the oxidative addition, Figure 88.

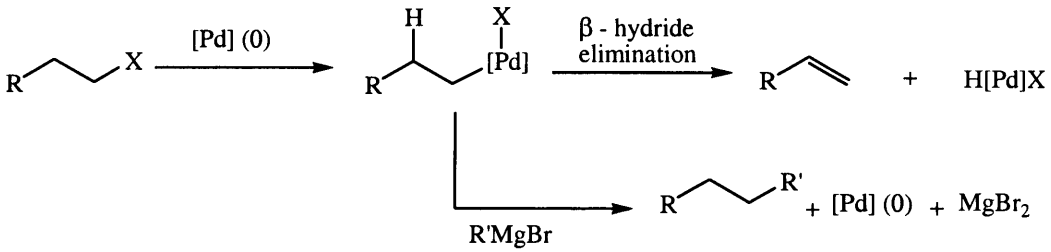


Figure 88

Initially, alkyl chlorides were chosen as coupling partners in conjunction with excess phenylmagnesium bromide[410] to aid with deprotonation of the NHC precursor. Using $Pd(OAc)_2$ (4 mol%), ligand (4 mol%) in NMP as solvent, with a 1.5:1 ratio of Grignard being added to the alkyl unit (*Pd catalysed Kumada coupling – Method A*), we were unable to effect coupling either at room temperature or elevated temperatures with any ligand. Substituting toluene as solvent in this reaction, which was a successful solvent for our Suzuki coupling experiments (Section 6.3), did not result in any coupled product

being recovered, and was similarly unsuccessful at temperatures up to 100 °C. Increasing the reactivity of the alkyl halide as a coupling partner by replacing the chloro group with a bromide and returning to the *Pd catalysed Kumada coupling – Method A* conditions resulted in one of the ligands demonstrating the ability to support the reaction. **287** resulted in an 8 % yield of 1-phenylheptane **304** at room temperature in 1 hour, when using phenylmagnesium bromide and 1-bromoheptane as substrates. Extending the reaction time or increasing the temperature had no effect on the outcome of the reactions, and the blank reaction produced no coupled product.

Substituting $Pd_2(dba)_3$ (4 mol%) as the palladium source (*Pd catalysed Kumada coupling – Method B*) resulted in an improved yield of 23% when using **287** in 1 hour, with the other ligands displaying no activity.

6.6.1 Interpretation of the results observed during the development of methodology for the dehalogenation of aryl halides.

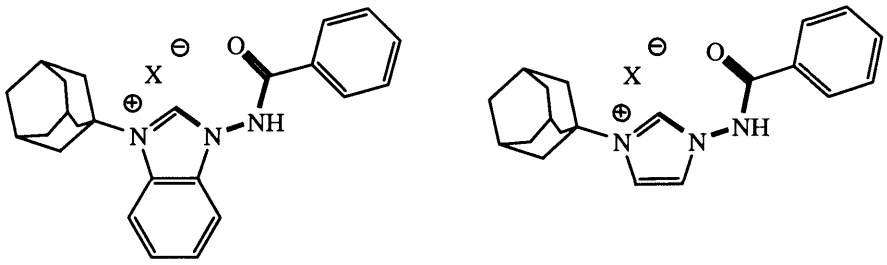
The Kumada coupling is in principal similar to the Suzuki coupling, oxidative insertion into an organohalide species, and transmetallation with the coupling partner, before reductive elimination to yield the product. As with the Suzuki reaction therefore we expect an electron rich metal to be important for insertion into the carbon halogen bond (especially in the case of C-Cl bonds), and a ligand with bulky *ortho* substituents to destabilise the transmetallated intermediate and promote reductive elimination. The dependence of the Kumada coupling reaction on the steric environment surrounding the metal is seen by ligands possessing very bulky substituents having a long association with the reaction.[411] The first general method for catalytic coupling reactions using alkyl halide substrates was described by Fu,[412] who performed palladium-catalyzed Suzuki reactions using tosylates as the coupling partner, whereas Kambe[413] reported on the efficient nickel-catalyzed Kumada coupling of 1-chlorooctane with n-butyl magnesium chloride in the presence of 50 mol% of 1,3-butadiene. Butadiene plays an important role in the reduction Ni (II) to Ni (0), *via* a Ni-butadiene complex, which is less reactive toward R-X but readily reacts with RMgX to form a reactive allyl intermediate. This activation of the Ni (0) by butadiene is also speculated to enhance its nucleophilicity towards R-X, thereby improving the rate of the reaction. Palladium-catalysed coupling reactions of alkyl chlorides have received relatively little attention, but Beller has recently reported the first palladium-catalysed Kumada reaction, using tricyclohexyl phosphine as ligand, which allows for the room temperature coupling of various aryl magnesium bromides with several functionalised and non-functionalised alkyl chlorides.[414] The main reason for the lack of research activity in Pd catalysed couplings which involve C-Cl bonds is the difficulty of overcoming the slow oxidative addition of the palladium to the C-Cl bond, and we had hoped that NHC ligands might overcome this problem. The most successful ligand precursor tested for Kumada coupling was **287**, which structurally, is the closest analogue to the current gold standard in the literature, **297**. Under identical conditions to those which resulted in 97% yield of the coupled product between heptylchloride and phenylmagnesium bromide using **297**, we noted only 8% of product, even with the more reactive alkyl bromide. The reduced activity of **287** can only be attributed to the reduced steric strain

imparted by the ligand *vs.* **297**. The imidazole ligands which we designed posses greater electron donating capacity than that of **297** and so should facilitate insertion into the strong C-Cl bond. We also know from our Suzuki studies (section 6.3) that **279** and **280** are capable of insertion into C-Cl bonds, and that **279** also achieved this feat in the nickel promoted dehalogenation (section 6.5). All of these ligands however fail. In both the dehalogenation and the Suzuki reaction where **279** and **280** were successful, a certain amount of steric freedom was required to accommodate the bulk of the substrate. However as previously established, the Kumada reaction requires bulky ligands. It is the role of the ligands to destabilise the *bis*organo-substituted palladium intermediate and promote reductive elimination. From the results of the Kumada coupling experiments we can only infer that **287** is more sterically demanding than either **279** and **280**, but as it is significantly less sterically demanding than **297**, this could account for the low turnover observed. The improved yield observed when using a Pd (0) source must be attributed to the greater ease of formation of the active catalyst, and hence its presence in the reaction solution for a greater amount of time and possibly in greater concentrations than in the case when a Pd (II) source is applied to the reaction, thereby explaining the improved yield.

6.7 Further discussion

6.7.1 Complex Synthesis

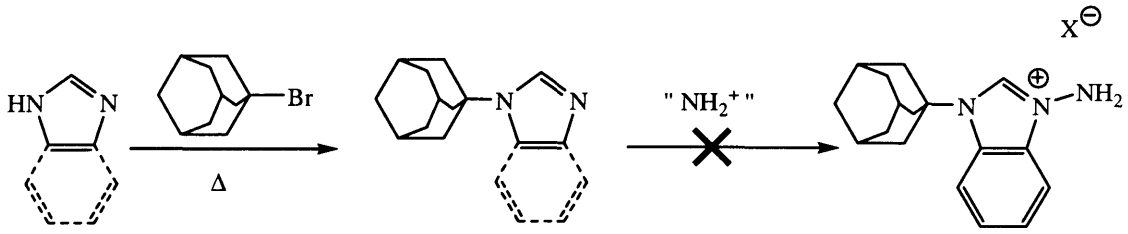
As part of our acac ligand range we wished to synthesise ligands possessing varying degrees of steric bulk and electronic properties, and to this end required a range of adamantyl-substituted complexes. The synthesis of imidazole derivatives such as **305** and **306** would result in molecules possessing an acac like chelate connectivity, with significant steric bulk as well as the electronic 'aza variation' in the link.



305 **306**

Figure 89

In the event however even although 'adamantylation' of imidazole and benzimidazole was achieved with 1-bromoadamantane to give the alkylated products **307** and **308**, we were unable to achieve amination of the resulting alkylated benzimidazole using the

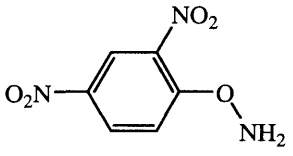


Imidazole **307**
Benzimidazole **308**

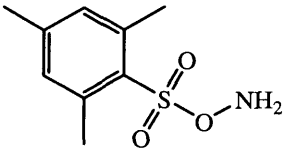
Scheme 70

common aminating agent hydroxylamine-O-sulphonic acid (HASA), Scheme 70. The amination reaction[415] failed as HASA is only soluble in aqueous solutions and the

substrates are only soluble in organic solvents, prompting us to synthesise two organic soluble aminating agents, 2,4-dinitrophenyl-hydroxylamine **309** and mesitylsulphonyl-hydroxylamine **310**.[416] Although these reactions were homogenous, no suitable conditions could be found which resulted in the amination of **308**.[417] Conditions were developed that led to isolation of the aminated sulphonic salt of adamantyl-imidazole **311** albeit in a low 12.4% yield.



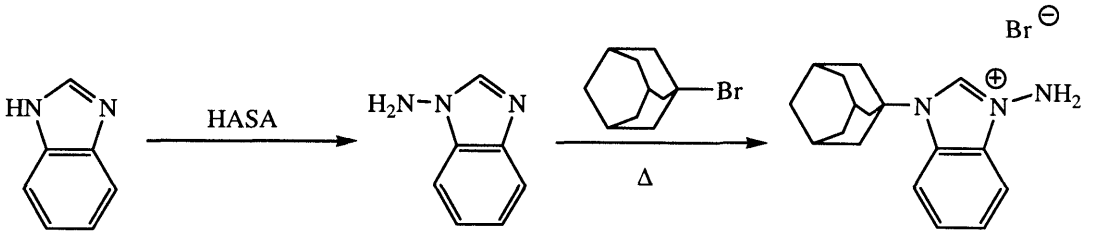
309



310

Figure 90

Amination of benzimidazole using HASA provided the corresponding *N*-amino derivative **312**, which, on treatment with 1-bromoadamantane, resulted in the alkylated *N*-amino imidazolium salt **313**, in 2.9% overall yield.

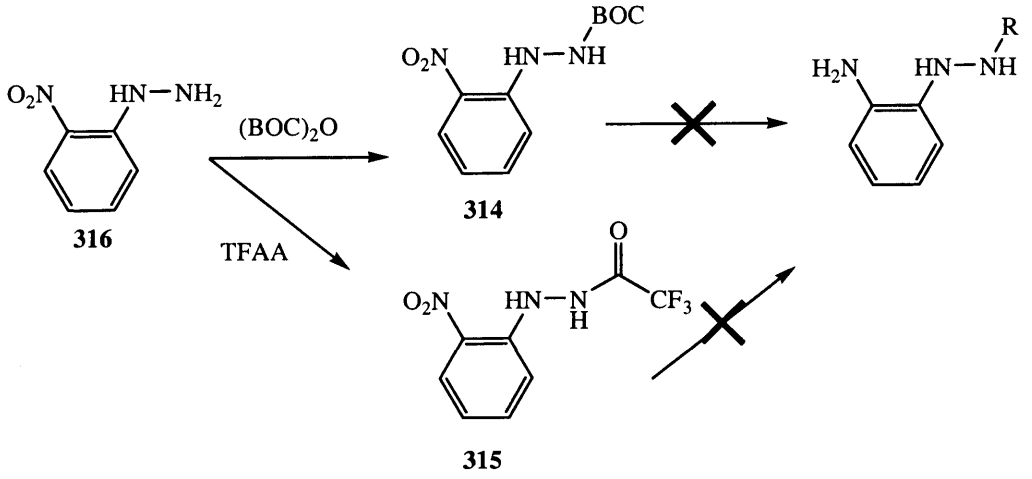


312
46%

313
6.3%

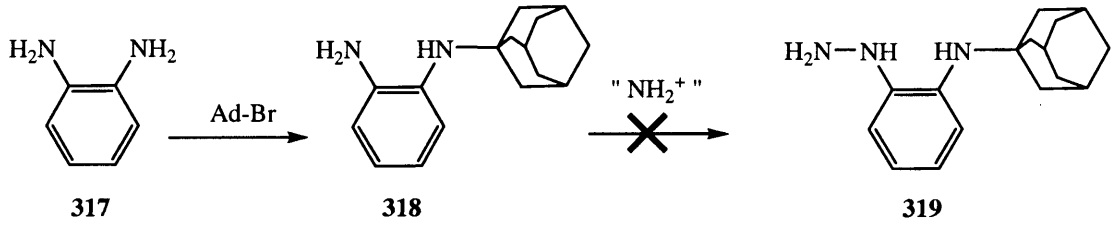
Scheme 71

Since such a low yielding synthesis of **311** and **313** was unacceptable, other routes were also investigated. Synthesis of the BOC (**314**) and trifluoroacetate (**315**) derivatives of 2-nitro-phenylhydrazine **316** was achieved, followed by the attempted reduction of the nitro group using Pd/C.[418] The route envisaged involved alkylation of the free amine, before cyclisation, to give the required product. However, conditions that could affect the reduction cleanly and in adequate yield were not found, Scheme 72.



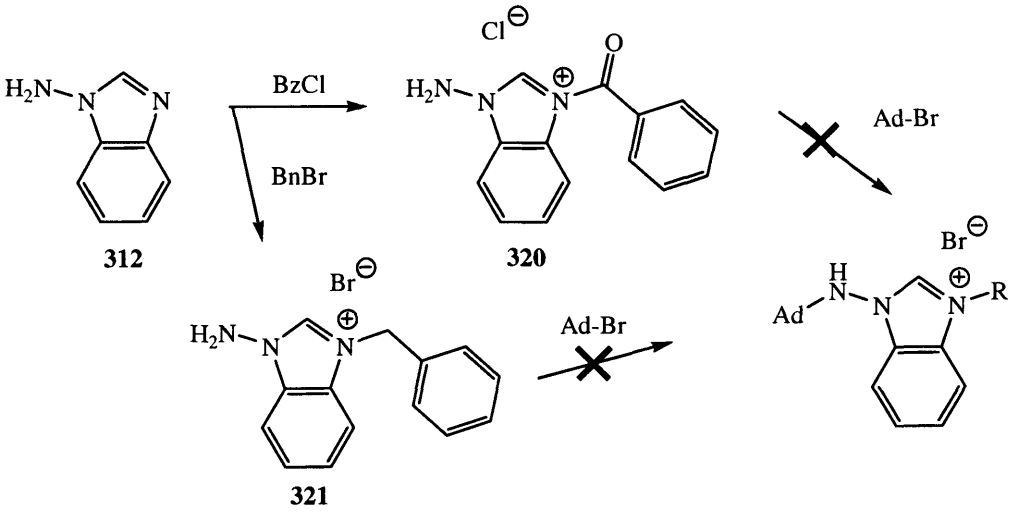
Scheme 72

In an alternative approach, alkylation of 1,2-diaminobenzene **317** with 1-bromoadamantane yielded the mono alkylated species **318**, but amination using HASA, **309** or **310** failed, thus precluding the planned cyclisation to **319**.



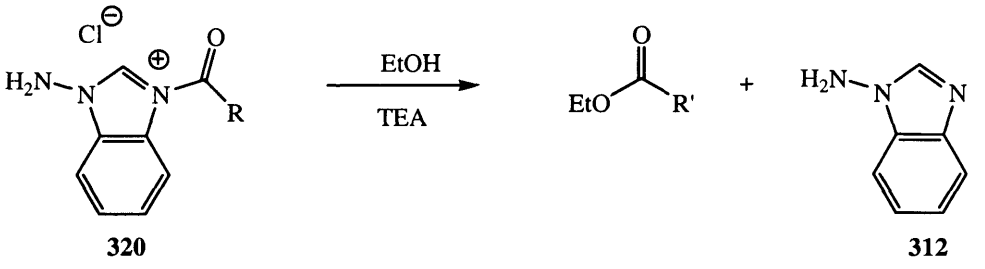
Scheme 73

In similar fashion, acylation of *N*-aminobenzimidazole **312** with benzoyl chloride resulted in the acylated product **320**, but further reaction of this species with adamantyl bromide failed. We initially felt this may be due to the electron withdrawing nature of the acyl group, and so replacement of this by a benzyl group, giving **321**, was achieved using benzyl bromide. However, **321** was also unreactive towards adamantyl bromide, Scheme 74.



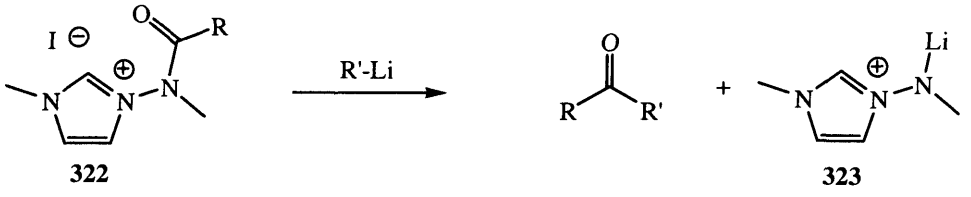
Scheme 74

A shortfall of a molecule such as **320** is that it quickly degrades to the parent aminobenzimidazole **312** in the presence of a nucleophile, Scheme 75. Species such as **322** have also been documented to degrade in a similar manner but in this case a strong nucleophile such as an organolithium was required, Scheme 76.[419]



Scheme 75

The synthesis of molecules containing an acyl group attached to a *N*-aminated imidazole such as **322**, is an approach that has been successfully applied by Alvarez-Builla to synthesise ketones, using organometallic reagents and the acylating species as featured in Scheme 76.[419]



Scheme 76

However, due to the difficulties encountered in the synthesis of adamantly substituted ligands, and the low yields of the 'successful' methods, it was decided not to pursue these species any further.

A second class of ligands which proved difficult to access were aryl substituted 4-amino-1,2,4-triazoles. The synthesis of 4-mesityl-1,2,4-triazole **324** was achieved using the simple condensation reaction between diformylhydrazine **325** and mesityl aniline. However, all attempts to *N*-aminate this species failed. The *N*-aminated product was required in order to expand our novel ligand range and as a method of reducing the reactivity of the ligand in the role of acylating agent.

6.7.2 Isolation of carbenes/metal complexes

The reason for our failure to isolate the free carbenes in this class of ligands is not fully understood. It has been documented elsewhere that other workers were unable to isolated the free form of similarly functionalised carbenes.[371] It can be imagined that one of the possible side reactions might involve intramolecular attack of the enolised carbonyl on the electrophilic C_1 position of the heterocyclic ring to give compounds such as **326**. Precedent for this type of reaction occurring with triazoles,[420] as well as benzimidazoles exists.[421]

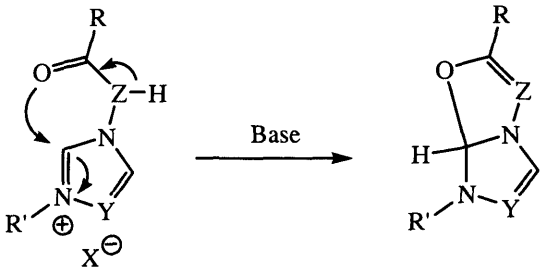
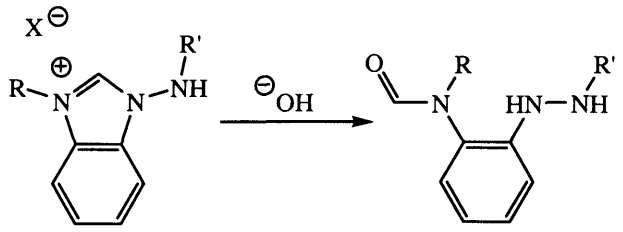


Figure 91

Although it was possible that the bicyclic systems such as **326** could undergo an α-elimination reaction to generate the desired *N*-heterocyclic carbene, it could also react further or decompose, as seen similar systems.[422] In the case where Z = NH, we postulated that *N*-alkylation might inhibit the cyclisation. Ligand precursors **278**, **282**

and **283** proved to be resistant to *N*-methylation, demonstrating the poor nucleophilicity of the hydrazone nitrogen, but conditions were found to methylate **281** and **283**. However it was found that the resulting alkylated species **327** and **328** were equally prone to decomposition when attempts were made to trap the anion with deuteromethanol.

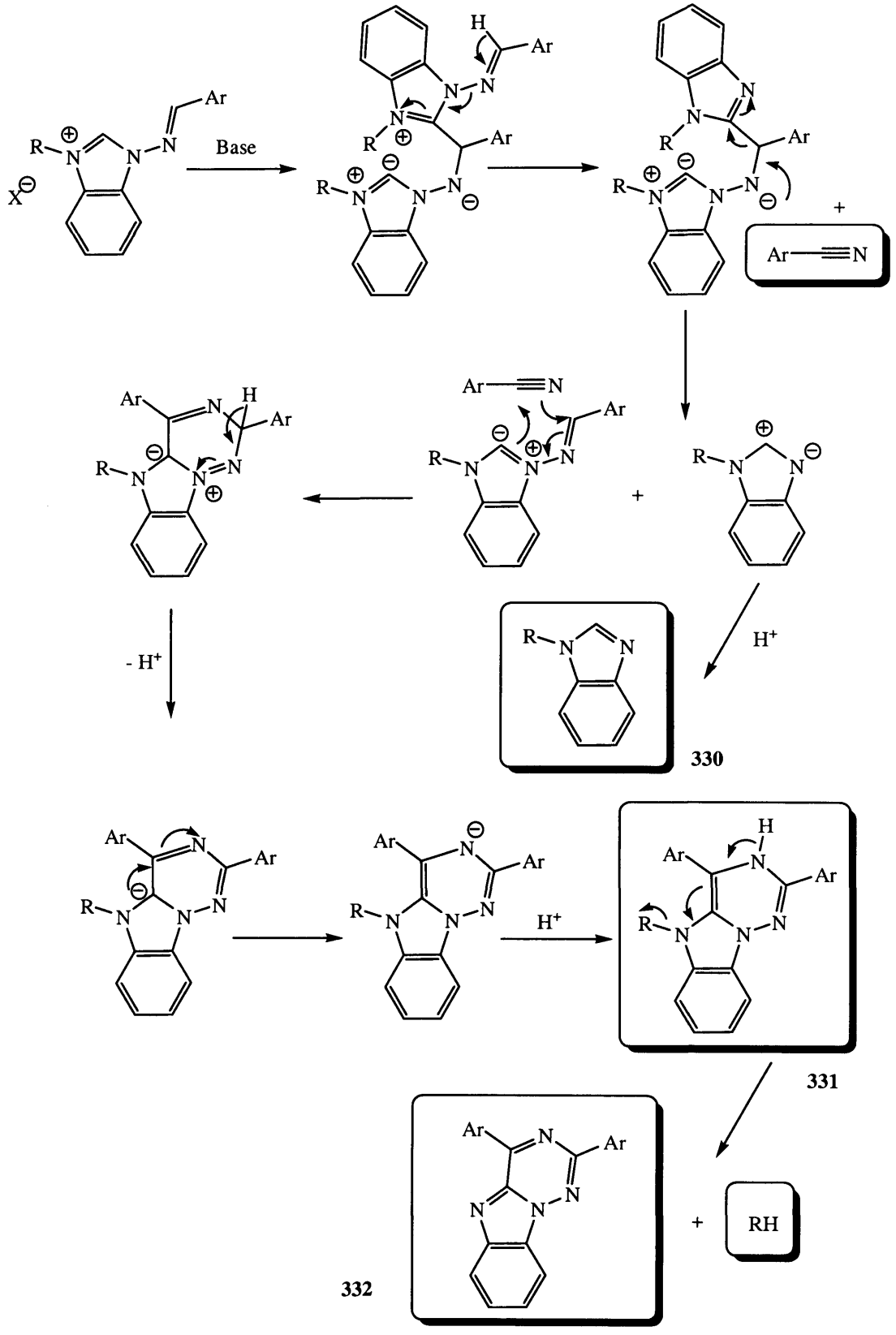
Further precedent exists for the degradation of this type of molecule under basic conditions, even in the presence of a relatively weak base such as TEA or K_2CO_3, whereby hydrolysis of the imidazolium ring occurs should trace amounts of water be present to give species such **329**.[423]



329

Figure 92

Further reports demonstrate that the N-N bond is thermally labile in some imidazole-derived cations and we believe that this instability can also be inferred for the triazole series with rearrangement of 1-acylamino-3-alkylbenzimidazolium salts into 1-alkyl-2-acylaminobenzimidazoles occurring under mild conditions.[424] Other reports demonstrate a similar decomposition pathway for 1-iminoamino-3-alkylbenzimidazolium salts[420b] such as **284** as detailed in Scheme 77.



Scheme 77

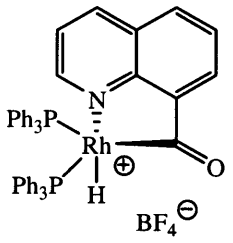
Deprotonation of molecules such as **284** result in a carbene, which can intermolecularly attack the polarised C=N bond of the azomethine fragment of a second molecule. This unstable intermediate rearranges to give the tricyclic compound **330** *via* the proposed formation of an arylnitrile fragment due to fission of the N-N bond. Formation of a molecule of alkyl-benzimidazole **331**, and the rather unlikely formation of the dealkylated tricycle **332** as depicted in Scheme 77 have all been proposed in the literature.[421b]

Chapter 7

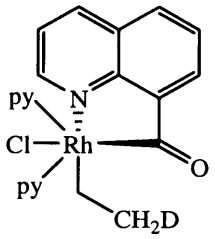
Hydroacylation

7.1 Introduction

The hydroacylation of alkenes, in which an aldehyde is added to a C-C multiple bond, generally in the presence of either a Pd, Ru or Rh complex, has the potential to be a powerful, atom-economic[425] tool for the synthesis of ketone containing products. It is an example of a growing number of transformations based on C-H bond activation,[426] but is currently underutilised due to a lack of suitable catalysts to promote the reaction. Tsuji, who noticed that Wilkinson's catalyst decarbonylated aldehydes, first postulated the concept of this reaction.[427] The mechanism proposed for hydroacylation involves oxidative addition of the aldehyde to a Rh (I) source, commonly Wilkinson's catalyst **334**, to give an acylrhodium (III) hydride. Olefin insertion to so formed Rh (III) hydride gives an acylrhodium (III) alkyl such as **336**, with reductive elimination furnishing the ketone. This mechanism has been validated by several studies confirming the presence of key intermediates, such as the isolation of the first stable acylrhodium-(III) hydride intermediate **335**[428] and the acyl-alkyl-rhodium-(III) intermediate **336**.[429]



335



336

Figure 93

One of the major issues facing researchers is the propensity of the key acyl-metal intermediates to undergo decarbonylation, which results in reduced substrates and inactive catalysts. Intermolecular hydroacylation frequently fails when catalysed by Wilkinson's catalyst because decarbonylation of the starting aldehyde is much faster than alkene coordination and subsequent hydrometalation to give the acyl-alkyl-Rh species e.g. **336**.[430] The possibility that an intramolecular process could enhance the rate of hydride-olefin insertion was therefore investigated and resulted in encouraging results.[431] Wilkinson's catalyst and its variants promote intramolecular hydroacylation but catalytic turnover is still low because of the competing decarbonylation, Figure 94.

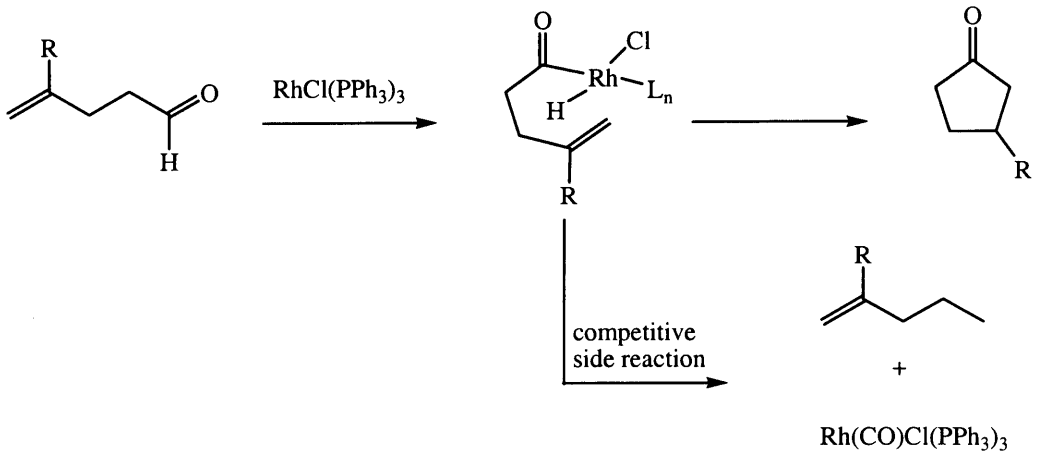
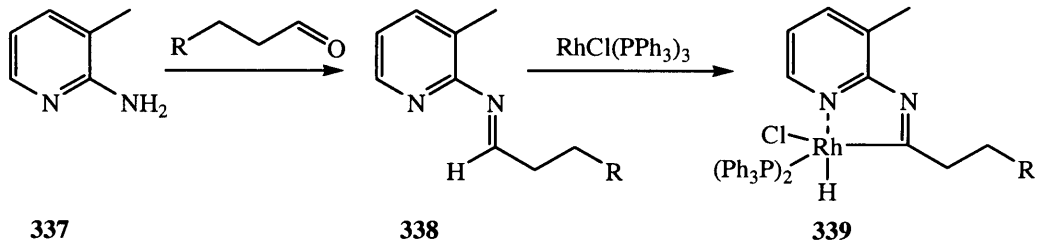


Figure 94

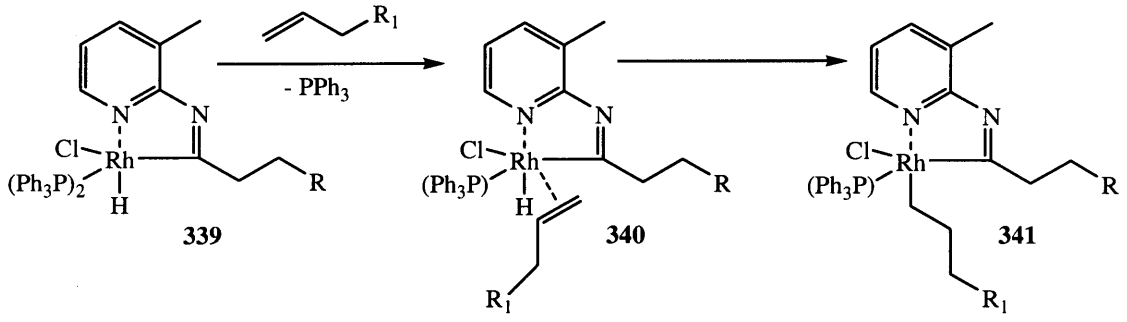
It is known that carbonyl ligands positioned *trans* to phosphine ligands are destabilised due to the *trans-effect*, and are even further destabilised if the complexes are cationic.[432] We believed that Rh (I) NHC complexes would be even better at destabilisation of carbonyl ligands, helping prevent the decarbonylation reaction, for the reasons discussed in the chapter dealing with transfer hydrogenation of aldehydes. Although intramolecular versions of the reaction have been developed and successfully employed for the synthesis of a range of cyclopentanone systems,[433] the synthesis of larger ring systems[434] and intermolecular reactions remain significantly more challenging.[435] An ingenious method of stabilising the rhodium centre to prevent competitive decarbonylation, was found to be achievable by chelation of the metal complex, with an early example of this strategy coming from Suggs, who used 2-amino-3-picoline **337**, as a chelating tether to support both the aldehyde and Wilkinson's catalyst.[436] The 2-methyl group of **337** is vital to formation of aldimine intermediate **338**, as without it, the corresponding aminal is the major product.[437]



337 **338** **339**

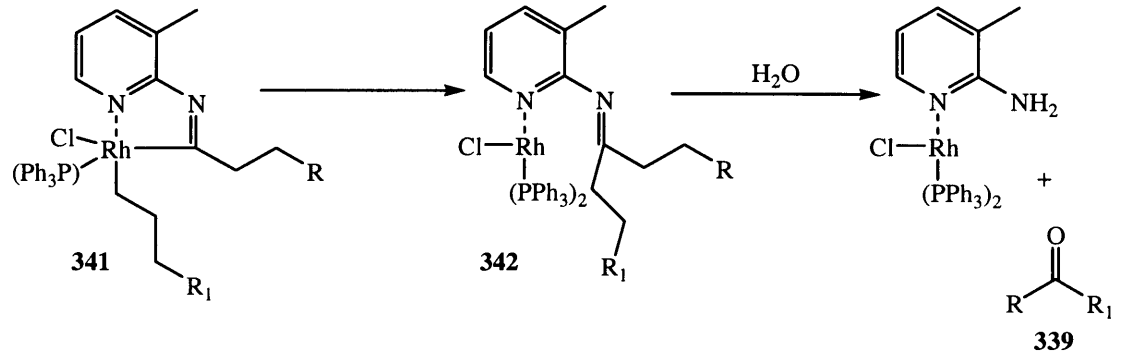
Scheme 78

The Rh (III) species **339**, which is sufficiently stable to allow for isolation and characterisation, is formed by the oxidative insertion of Wilkinson's catalysts to the aldimine formed between **337** and an aldehyde substrate. Coordination of an alkene to the Rh (III) complex **339**, leads to a hydrometalation of the alkene and subsequent formation of an acyl-alkyl-Rh (III) intermediate **341**.



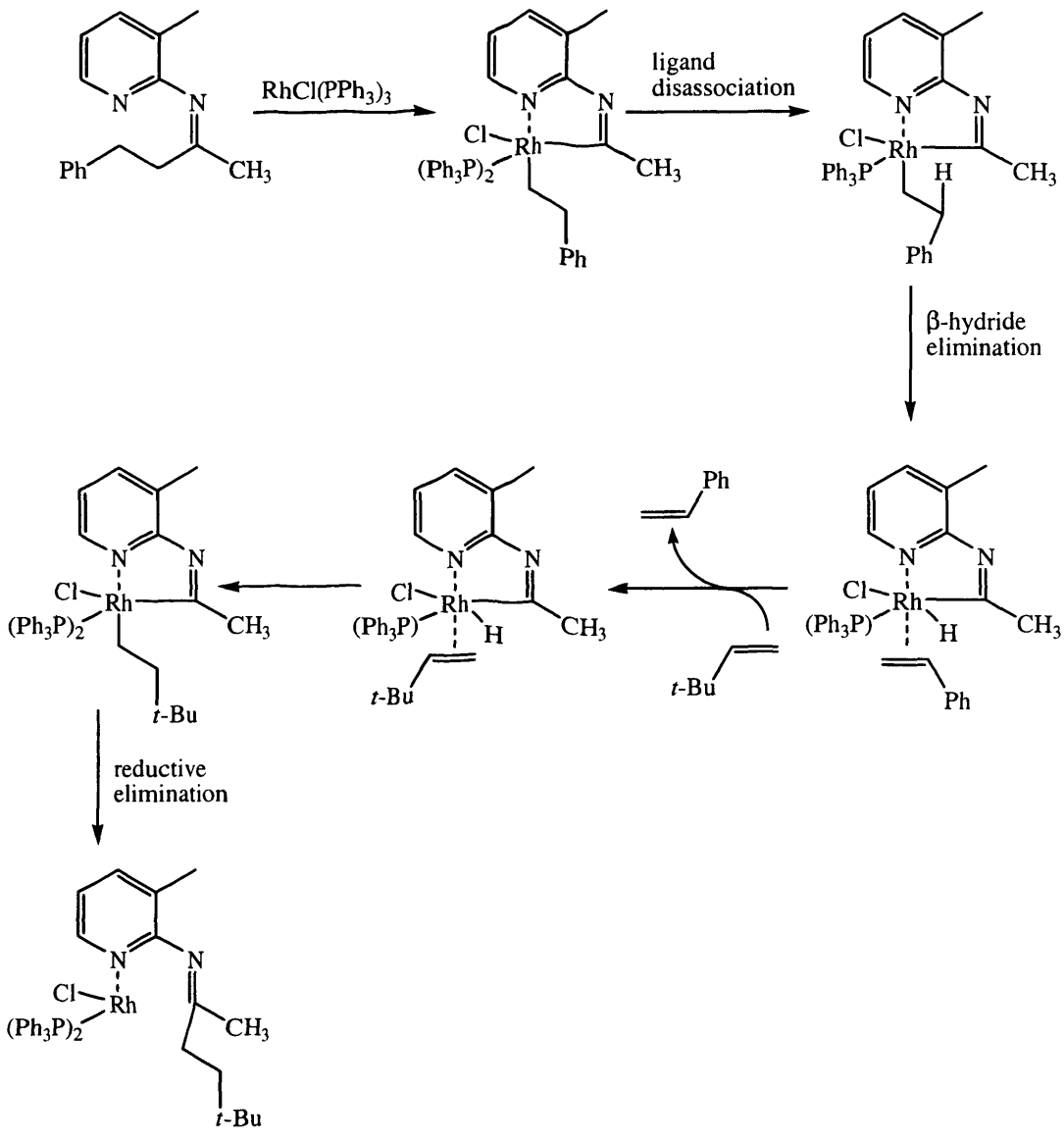
Scheme 79

A reductive elimination reaction forms **342** and hydrolysis of this ketimine by water present in the reaction mixture due to the prior condensation reaction which furnished aldimine **338**, leads to the ketone product **339**.



Scheme 80

This early research was developed upon by Jun in a series of papers in which he uses 2-amino-3-picoline as a tether to promote both the intra- and intermolecular hydroacylation of alkenes and alkynes.[438] An interesting extension of the hydroacylation methodology involves the activation of C-C bonds,[438] offering a novel method capable of replacing an R group of a ketone with a new R' group from a suitable donor, Scheme 81.



Scheme 81

The yield under Jun's conditions for the hydroacylation of 1-hexene and benzaldehyde occurs quantitatively, whereas 4-methoxy- and 4-trifluoromethyl-benzaldehydes give 79% and 71% of hydroacylated product respectively, in 1 hour, at 130°C.[438c]

Other techniques have also been found to minimise the decarbonylation reaction during both the intra- and intermolecular reaction. Willis demonstrated that a pendant heteroatom produces chelated acyl-metal intermediates that are resistant to decarbonylation but disposed to hydroacylation,[439] and when coupled with cationic Rh (I) sources offer high yields between β-methylsulfanyl aldehydes and functionalised alkenes such as acyrlates, styrene's and sulphones. Bendorf used a similar method of

heteroatom chelation to affect intramolecular hydroacylation between alkenes or alkynes and produced polycyclic systems in good yields,[440] whereas Tanaka has employed a double chelation method to facilitate intermolecular hydroacylation between salicylaldehydes and 1,5-hexadienes, under remarkably mild reaction conditions, affording a mixture of *iso*- and *n*-hydroacylated products in good yields (Figure 95).[441]

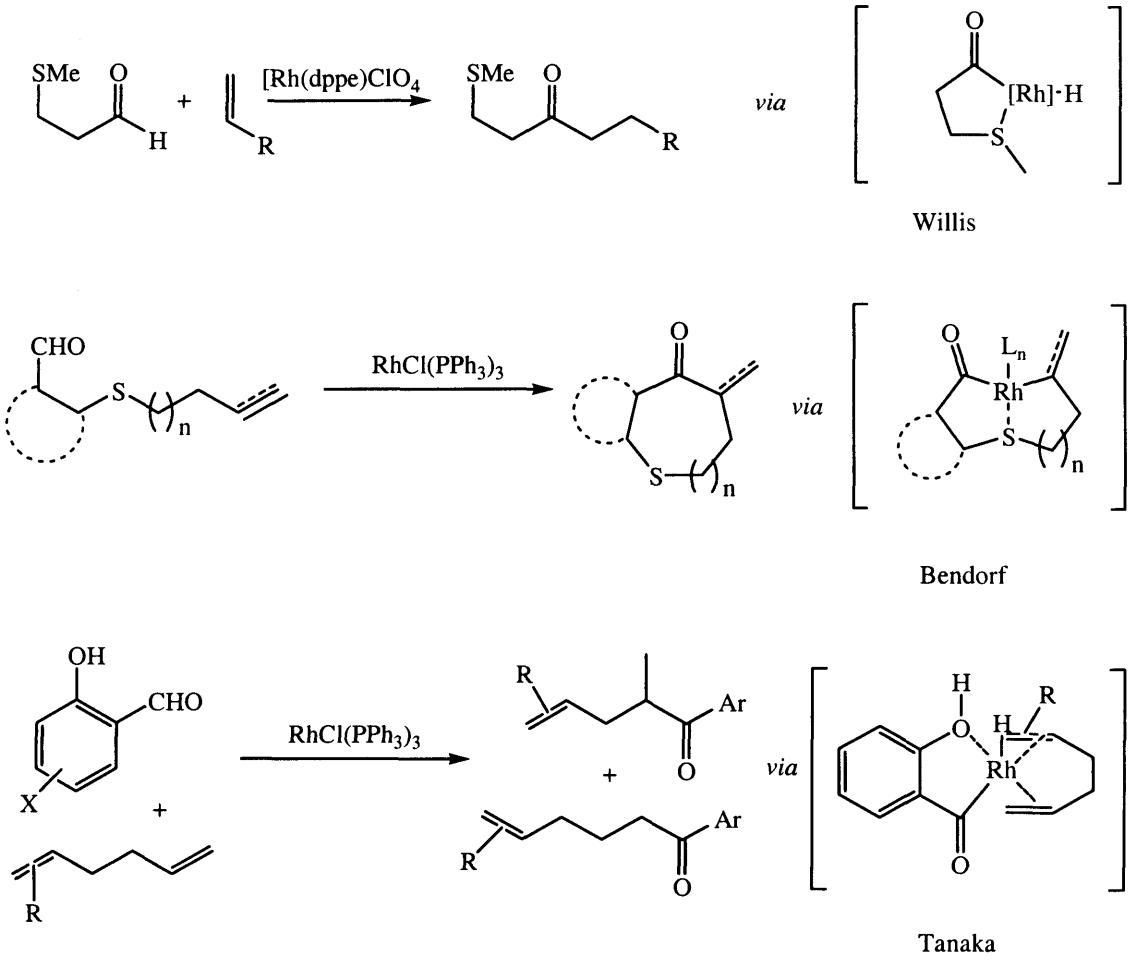
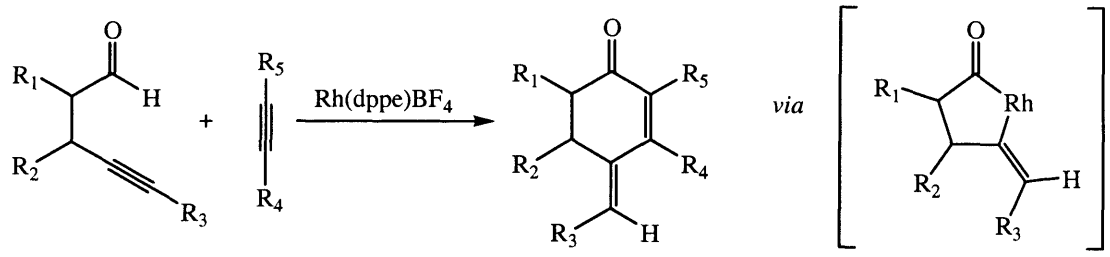


Figure 95

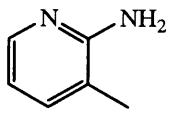
In the intramolecular variant Fu has also made significant contributions to this field with a novel method to access highly functionalised cyclopentanones and cyclohexanones, Figure 95.[442]



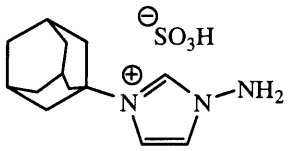
Scheme 82

7.2 Results of Hydroacylation experiments

Consideration of the approach of Jun and coworkers suggested to us that replacement of the chelating pyridyl nitrogen of 2-amino-3-picoline by an NHC unit could create a more robust catalyst which would also be less prone to decarbonylation. To our knowledge, there is no example of a hydroacylation reaction facilitated by a ligand incorporating a NHC moiety. A range of ligands was accordingly synthesised, each incorporating an NHC precursor and a pendant amine functionality for substrate aldimine formation, and with similar geometric relationship to that of 2-amino-3-picoline, Table 26.



337



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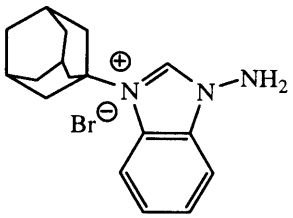

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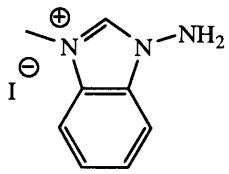

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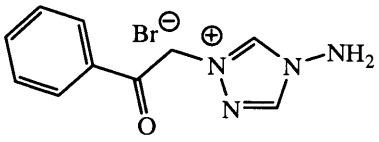

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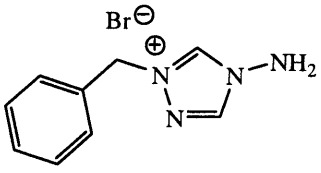

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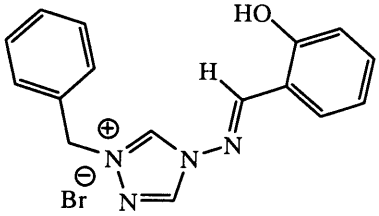

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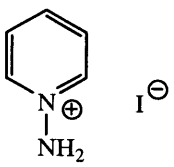
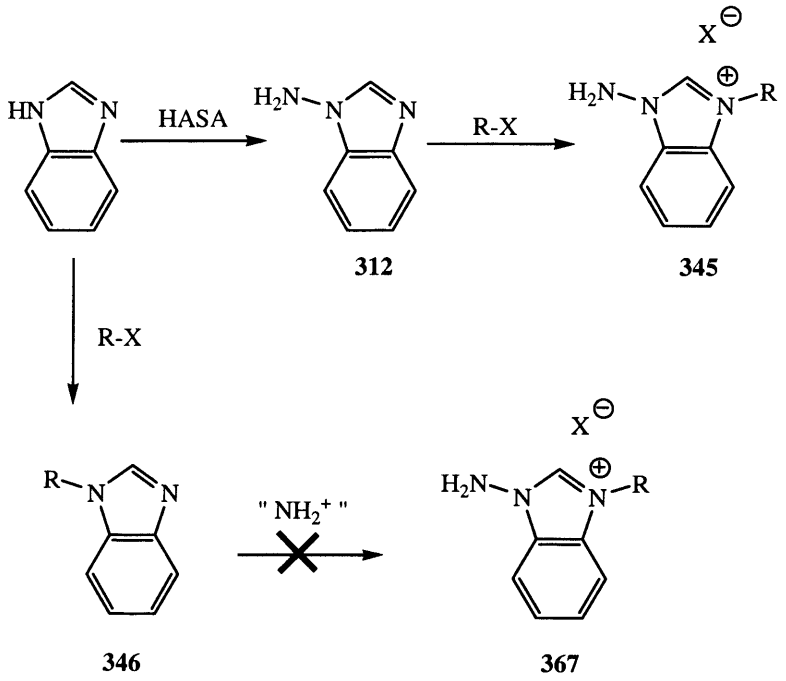


344

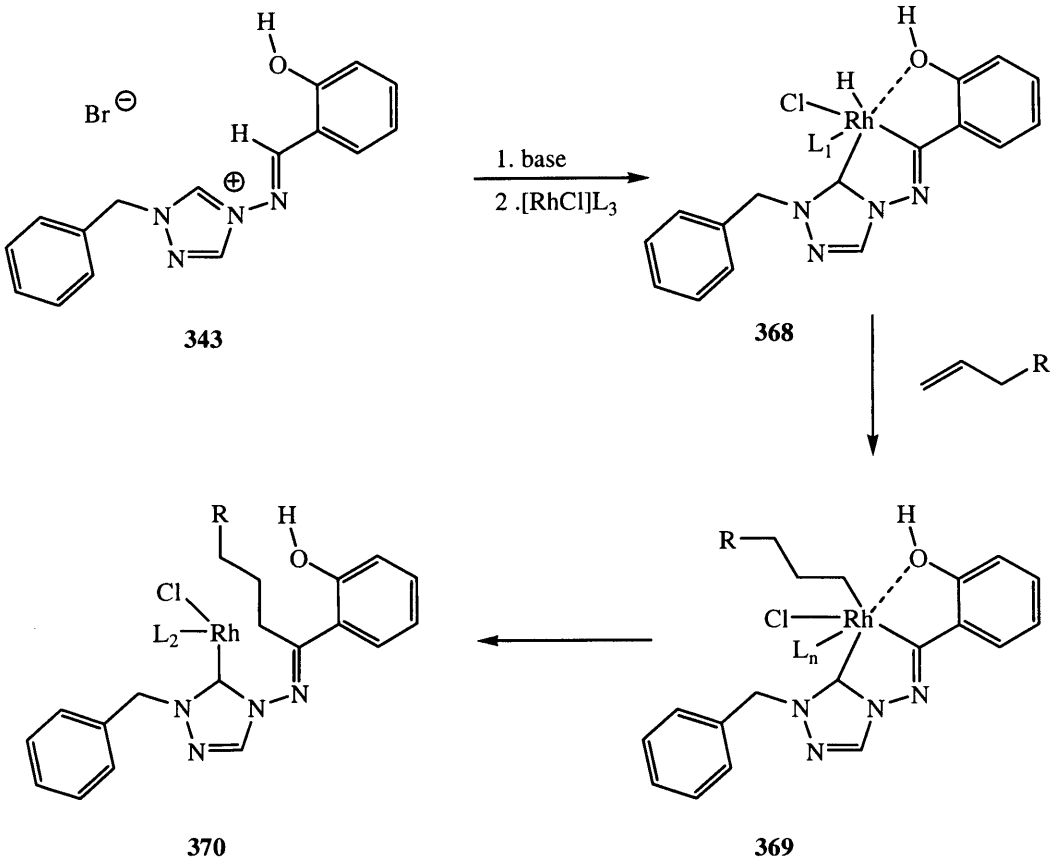
Table 26

As with the acac mimic range of ligands, a variety of NHC precursor scaffolds were studied in order to modulate electron donation to the metal centre, with alkyl imidazoles being the most strongly donating, and decreasing through the benzimidazoles to the triazoles, which are the weakest donors. Synthesis of these ligands can only be achieved by amination of the parent heterocycle (in the case of imidazole and benzimidazole), alkylation to produce the corresponding salt, and further functionalisation if required. Reversal of the amination-alkylation order results in failure, Scheme 83.



Scheme 83

A further modification, incorporated into ligand **343** is the phenolic hydroxyl group, which was designed to investigate a particularly ambitious idea. Similar to the work of Tanaka[441] the idea was to use the phenolic OH, but in this case a highly strained intermediate **368** is generated, which may facilitate the subsequent steps. Initially, this ligand was synthesised with inclusion of the salicaldehyde fragment, in order to encourage rapid formation of **368**, and as such can be viewed as a 'stoichiometric ligand', Scheme 84.



Scheme 84

Once the concept was validated, we intended to investigate the addition of sub-stoichiometric quantities of the parent triazolium ligand to a reaction mixture containing salicaldehyde as an independent moiety, forming **343** *in-situ*. Unfortunately however, no activity was ever seen with this particular ligand.

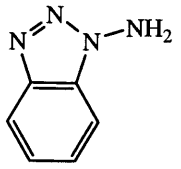
Ligand **344** was synthesised to enable us to measure the effect on the reaction of using a carbene to chelate to the metal *vs.* the simple reaction between the solvated ruthenium complex and an aldimine.

Attempted silver complex formation with the ligands detailed in Table 26 using the methods referenced in chapter 6 (acac mimics) failed, and the use of bases such as *tert*-BuLi, KHMDS or KH resulted in decomposition of the molecules, most likely *via* one of the methods also discussed in chapter 6. Methods to form the rhodium carbene complex directly from Wilkinson's catalyst **334**, or $[RhCl(COD)]_2$ with the precursor

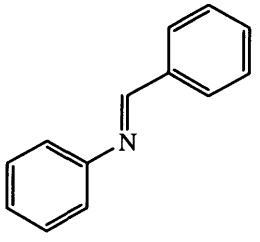
ligand salts listed in Table 26 were unsuccessful, even though similar methods have been applied to **294**.[443]

The conditions of Jun[438c] involve combining the aldehyde substrate (1.0 eq), 2-amino-3-picoline (0.2 eq), benzoic acid (6 mol%), aniline (0.6 eq), and the alkene substrate (5.0 eq) in toluene with stirring for several minutes to allow aldimine formation, followed by addition of Wilkinson's catalyst (2 mol%) and subsequent heating to 130 °C in a sealed vessel for one hour. The product is isolated by column chromatography. The role of aniline is to form an aldimine with the starting aldehyde, and this is catalysed by the benzoic acid. Once this has been achieved, rapid transimination to the picoline ligand is believed to occur, with the purpose of the transimination step being to ensure a continuous source of picoline aldimine, which results in an accelerated reaction rate.

Direct replacement of 2-amino-3-picoline **337** as used by the literature conditions with the ligands from Table 26, either in equal (0.2 eq) or twice (0.4 eq) literature quantities, in anticipation of forming the mono- or *bis*-NHC ligated Rh-complex *in-situ*, resulted in no hydroacylated product being detected, even when the reaction time was extended to 24 hours. To investigate at which point the reaction was failing, another ligand, 1-aminobenzotriazole **371,** was synthesised. Although this does not posses a carbene functionality, it can chelate to the rhodium in a similar manner to 2-amino-3-picoline to act as a model during our investigations. This removed the variable of carbene formation, allowing us to investigate the condensation-transimination steps involved in the reaction. Repeating the reaction using the conditions of Jun as before, but using 1-aminotriazole **371** as ligand (0.2 eq), resulted in only starting materials and **372** being recovered, with no benefits seen with extending the reaction to 24 hours.



371



372

Scheme 85

The results of this reaction inform us that the intermediate aniline aldimine **372**, forms with the substrate aldehyde, but transimination to our ligand does not occur. We are aware that the amino functionality of this type of ligand is not very nucleophilic due to the difficulties we experienced in alkylating similar *N*-amino based structures in our acac mimic studies. We explored the possibility that pre-formation of a stoichiometric amount of benzaldehyde aldimine with a volatile amine could benefit the reaction, by driving the equilibrium to favour formation of the substrate-ligand aldimine. Application of propylamine for the role of volatile amine (boiling point 48 °C[444]) was not successful as no transimination was observed *via* ^{1}H-NMR when **373** was refluxed in an open vessel in toluene, for 12 hours, in the presence of benzoic acid.

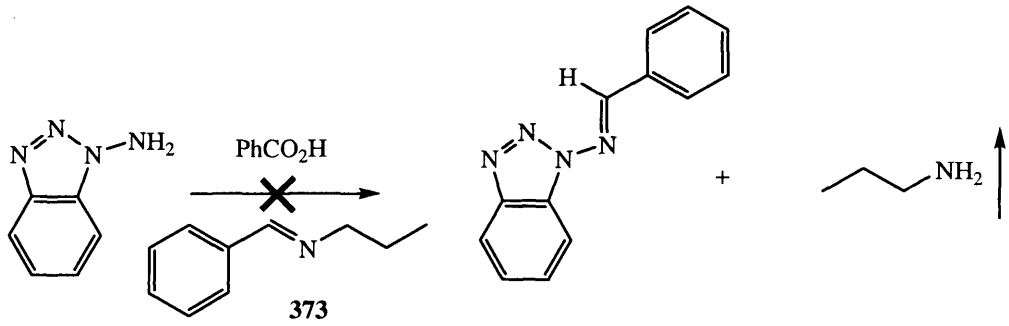


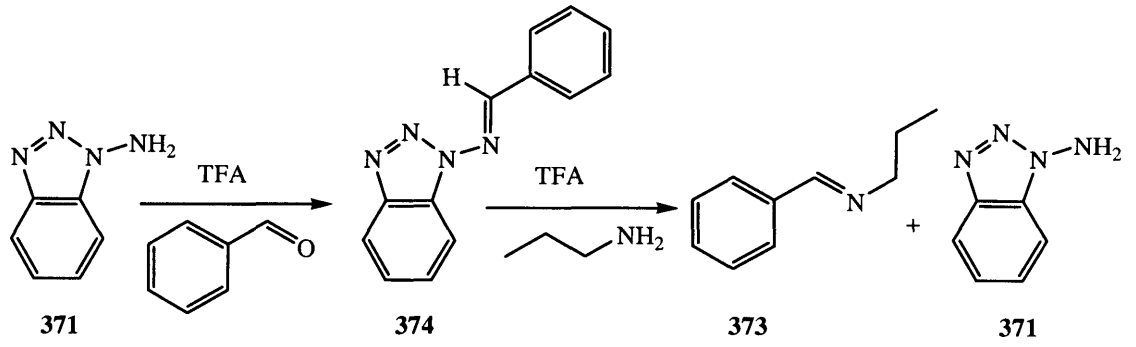
Figure 96

The original conditions in the literature employed benzoic acid as the acid catalyst, which has a pK_a of 4.2 (water), and as it did not appear to catalyse transimination with ligand **371**, we investigated the rate of imine formation/transimination under a range of acid conditions, Table 27.[445]

Acid	**pK_a (Water)**
CF_3SO_3H	-14
CH_3SO_3H	-2.6
CF_3CO_2H	-0.25
CH_2BrCO_2H	2.86
$PhCO_2H$	4.2

Table 27

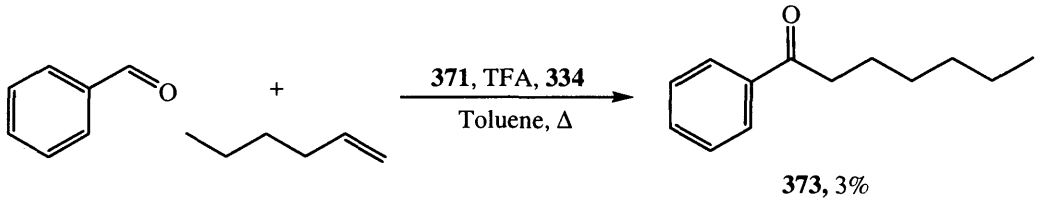
Addition of a 1:1 ratio of propylamine to benzaldehyde in C_6D_6 results in near spontaneous formation of the corresponding imine and an equivalent of water. Introduction of aminobenzotriazole **371** to this solution results in no transimination as evidenced by ^{1}H-NMR, even after addition of 0.1 equivalent of each acid from Table 27 to a fresh sample of the so formed propyl-imine **373** and stirring for 60 hours at room temperature. A similar lack of reactivity of **371** towards transimination was observed when **373** was replaced by **372** and the acid catalysis experiments repeated. As this model ligand was showing a remarkable lack of reactivity towards transimination reactions, we set out to develop conditions that would lead to the direct formation of an aldimine between **371** and the aldehyde substrate avoiding this troublesome step. Treatment of **371** with 1 equivalent of benzaldehyde results in no imine formation, but addition of TFA (0.1 equivalent) catalysed the condensation to an extent, with 56% imine formation (^{1}H NMR) after 60 hours. TFA was the only acid found which leads to aldimine formation, and increasing its concentration only reduces the rate of the condensation, presumably due to a greater percentage of the amine being protonated. Addition of 1.0 equivalents of propylamine to **374**, formed *via* TFA catalysis, results in rapid transimination from the ligand to the primary alkyl amine, destroying the required intermediate for the reaction, Scheme 86.



Scheme 86

These experiments confirm that the reaction fails under the original literature conditions, because the aldimine between the ligand and aldehyde substrate does not form. Since TFA was capable, to a limited degree, of catalysing imine formation with the model ligand, 1-aminobenzotrizaole and benzaldehyde, we therefore decided to apply this imine formation protocol to the range of ligands developed for this transformation. Unfortunately however, the only reaction, which produced

hydroacylated product, was that which contained the model ligand (0.2 eq), Wilkinson's catalyst (2 mol%), TFA (0.1 eq), 1-hexene (5 eq) and benzaldehyde (1.0 eq) resulting in a 3% yield of hydroacylated product **375** after 12 hours in toluene at 130 °C (*Hydroacylation method A*), Scheme 87.

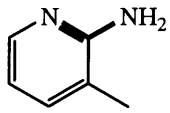


373, 3%

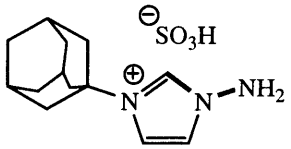
Scheme 87

7.3 Discussion of results from Hydroacylation experiments

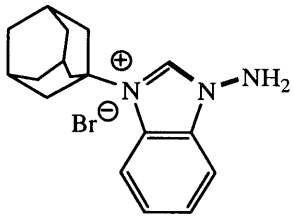
Although there is literature precedent for the formation of rhodium carbenes under *in-situ* conditions it is usually achieved by refluxing of the rhodium source with the carbene precursor in toluene,[446] or by use of a nucleophilic base such as KO^{t}Bu.[447] Our salts are insoluble in toluene and it is quite likely that strong nucleophilic bases such as those used in the literature, cause degradation of the ligands as discussed in Chapter 6.



337



311



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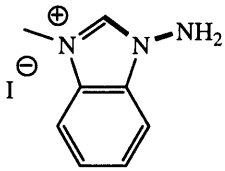

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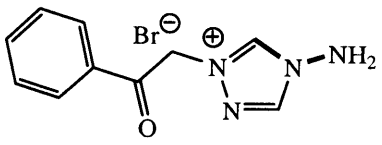

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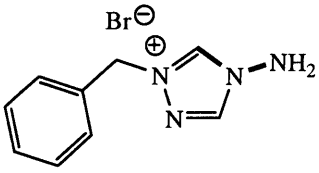

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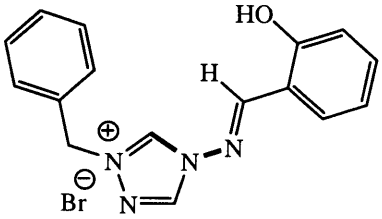

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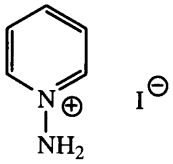
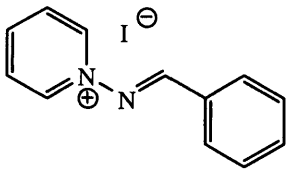


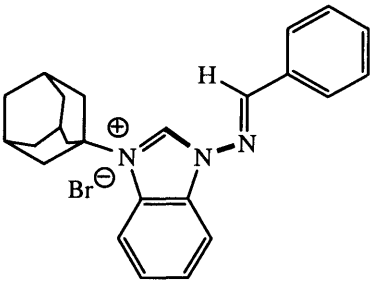
344

Table 26

1-aminobenzatriazole **371** is capable of chelating the rhodium complex to a limited extent during the reaction, without the need for carbene formation, as evidenced by the small yield of hydroacylated product. The other ligand precursors (Table 26) we synthesised however are incapable of supporting the metal centre until they have been converted to a carbene. It would appear from the lack of product, that under the conditions of the reaction, carbene formation does not occur with any of the ligands investigated. Confirmation that the reaction cannot proceed without Rh-chelation, is seen by the reaction of the preformed benzaldehyde aldimine of **376** under the typical reaction conditions (*Hydroacylation method A*). **376**, is incapable of chelating to the Rh, and no hydroacylated product was detected, even after 24 hours. Subjection of **378**, the aldimine of **313**, to the typical reaction conditions (*Hydroacylation method A*) should furnish product if *in-situ* formation of the carbene occurs. The reaction however resulted in no hydroacylated product, even when using stoichiometric amounts of Wilkinson's catalyst, demonstrating that the cause of the reaction failing is the inability of the ligand to complex the Rh species, giving us clear evidence that the carbene is not forming.



376



378

Figure 97

The fact that we recover a small yield of product using **371**, which is geometrically similar to the salts we synthesised, demonstrates that the ligand structure is such that the Rh atom is held in a suitable position to insert into the CH bond of the aldimine and that the alkene is capable of coordinating and reacting. Therefore, should conditions be developed that allow the formation of the carbene, active catalysts based on the structures we have produced will most likely be realised.

Chapter 8

Conclusions - Perspectives

We have developed versatile methodology for the transfer hydrogenation of ketones and more importantly, the more challenging aldehyde based substrates. The method takes advantage of the very cheap and safe to handle propan-2-ol as a hydrogen source. The use of a solid base makes for a very simple work up procedure; filtration through a plug of silica and removal of solvent. If the reaction has gone to completion, this provides a clean product without the need for further purification. The catalyst loading of 0.03 mol% is very low, offering respectable TON's and workable TOF's.
The slower formic acid/TEA azeotrope transfer hydrogenation method has the advantage of being essentially unreactive towards ketones due to the ligand exhibiting a size selective coordination pocket, selectively reducing aldehydes as demonstrated by competition experiments and the yields for individual examples. The requirement for higher temperatures, longer reaction times, and the acidic nature of these reaction conditions make this method less attractive, but still valuable for its chemoselectivity.

In the field of oxidation, we have developed several methods capable of oxidising a wide variety of substrates, under very mild conditions. Using NMO as stoichiometric oxidant resulted in excellent yields with no over oxidation to the acid product. Use of the alternative oxidant, TCCA, offers similarly good yields but with the possibility of driving the reaction to the oxidation level of an acid. Neither method was very successful with unactivated primary alcohols, but the use of NMO offers a limited degree of success for these more challenging substrates.

A range of novel ligands have been synthesised and shown to be capable of supporting a variety of reactions. With the knowledge of a reaction mechanism it is possible to select a ligand with the correct balance of electronic and steric properties for optimal activity. It is abundantly clear that it is possible to tune a ligand to have the precise physical/chemical properties required by the reaction, and in doing so, reactions previously thought difficult, become facile. However with this ability to tune so precisely the properties of a ligand comes the problem than an infinite amount of variation is possible. The success of any catalyst system strongly depends on its availability and hence on convenient methods for its preparation, and for this reason *in-situ* formation of complexes is amongst the most attractive of methods. The 'iminohalide method' attempted by us, and achieved in the case of simple *bis*alkyl substituents by Fürstner[448] also holds potential to be an excellent method to access NHC

based complexes without having to isolate and handle the sensitive free carbene. We have seen from the screening reactions carried out that no one ligand consistently out preformed the others. It is the belief of the author that the organic chemistry community is better served by having a small selection of simple to produce, active, multipurpose ligands rather than a raft of very active, single application metal, specific ligands. What becomes very clear when surveying the literature (and the chemical catalogues) is that the most effective ligands and hence the most widely applied are very simple in structure, Figure 98 shows the most commonly used NHC based ligands.

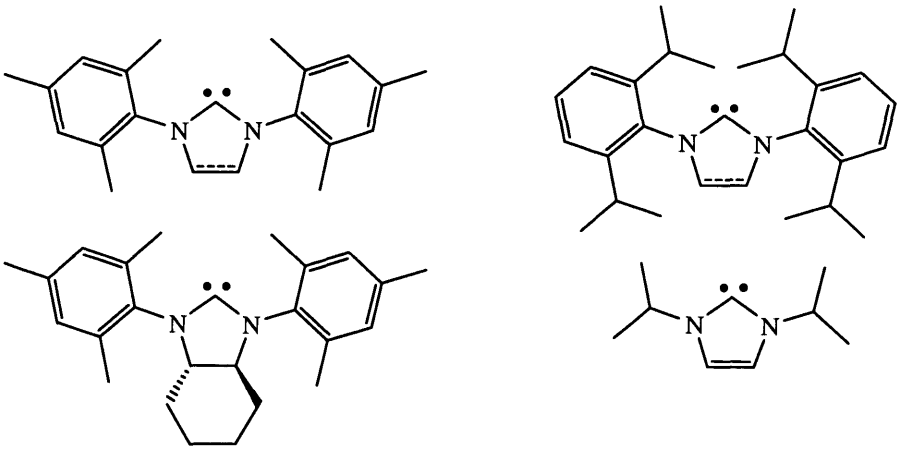
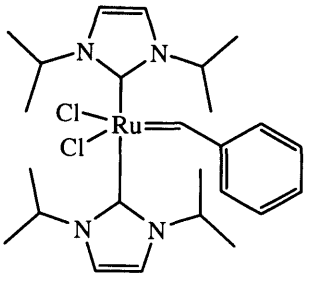


Figure 98

In fact the most widely used carbene ligand, and structurally the simplest is now incorporated in the instantly recognisable later generation Grubbs catalysts **333**.



333

Figure 99

Work on developing catalysts capable of activating C-Cl bonds still requires significant research. The feedstocks of the chemical industry containing C-Cl bonds are much

more abundant and significantly cheaper than the bromo- or iodo- analogues. They are also much more atom economical as a chloride atom will account for a substantially smaller portion of the total mass of the molecule relative to that of a bromide or iodide. Unfortunately the high C-Cl bond strength compared with C-Br and C-I bonds disfavours oxidative addition, the first step in catalytic coupling reactions, making the coupling of such substrates far more challenging.[449] It is in this area that NHC based ligands are ideally poised to provide a solution.

For the field of hydroacylation a second range of novel ligands were developed. Methodology was developed that shows the reaction to be achievable, but shortcomings in the formation of the active catalytic species were found. Should conditions be developed that allow the formation of the carbene, active catalysts based on the structures we have produced will most likely be realised.

Chapter 9

Experimental

General procedures

All reactions requiring the use of anhydrous/anaerobic conditions (including the preparation of all organometallic compounds unless otherwise stated) were carried out on a Schlenk line under an atmosphere of nitrogen, with solvents being degassed *via* a nitrogen purge before use. Glassware was pre-dried in an oven (110 °C) or flame dried and cooled under nitrogen prior to use. Stirring was by internal magnetic follower unless otherwise stated. All reactions were followed by TLC, where applicable, and extracted organic phases were dried with anhydrous magnesium sulphate unless otherwise stated.

Materials sensitive to atmospheric conditions were stored in a glove box under a dry nitrogen atmosphere, maintained by a recirculator with an activated copper catalyst for removal of oxygen and molecular sieves for moisture removal.

Diethyl ether, tetrahydrofuran and toluene were distilled from sodium with benzophenone ketyl as indicator immediately before use. Dichloromethane, petroleum spirit and triethylamine were distilled from calcium hydride before use. *Iso*propanol and *tert*-butanol were distilled from calcium hydride under reduced pressure and stored over activated 3Å molecular sieves prior to use. Methanol and ethanol were distilled from magnesium turnings and iodine under nitrogen, either directly into the reaction vessel, or stored and kept for later use over activated 3Å molecular sieves. Sodium and potassium hydrides were washed with petroleum spirit 30 – 40 °C until oil free, prior to use. Triphenylphosphine was recrystallised from methanol and dried *in-vacuo* prior to use.

Purification was carried out by column chromatography using the flash column chromatography technique reported by Still.[450] The silica gel used was Merck 60 (230-400 mesh). Thin layer chromatographic analysis was carried out using Merck aluminium-backed plates coated with silica gel 60 F_{254}, with components visualised using ultraviolet light, iodine, ninhydrin or ceric ammonium molybdate stain. All melting points were determined on a Reichert Thermovar hot stage device and are

uncorrected. Infrared spectra were recorded on a Perkin Elmer 1605 FTIR spectrophotometer using nujol mulls on NaCl plates or as KBr discs.

^{1}H NMR and ^{13}C NMR were recorded on a Bruker AC300 spectrometer operating at 300 MHz for ^{1}H, 75 MHz for ^{13}C, and 282.2MHz for ^{19}F, a Varian VXR400 operating at 400 MHz for ^{1}H, 100.5 MHz for ^{13}C and a Bruker Avance 500 operating at 500 MHz for ^{1}H, 125.7MHz for ^{13}C and 202.4MHz for ^{31}P. Chemical shifts (δ_H, δ_C, δ_F, δ_P,) are quoted as parts per million downfield from 0, and calibrated either using tetramethylsilane or the residual solvent peak as an internal standard.[451] ^{31}P chemical shifts are calculated relative to phosphoric acid. The multiplicity of a ^{1}H NMR signal is designated by one of the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sep = septet, br = broad and m = multiplet. Coupling constants (*J*) are reported as found, splittings on each individual resonance, are expressed in Hertz, and are quoted to the nearest 0.1 Hz. NMR solvents; C_6D_6 was dried over Na/K amalgam, and CD_2Cl_2 dried over 3Å molecular sieves, before being distilled *via* a freeze/thaw trap-to-trap process, and stored in a glove box.

Both low and high-resolution mass spectra were carried out at University College, London. Mass spectra were collected using a Micromass 70-SE magnetic sector mass spectrometer. Samples were ionised electronically (EI), with an accelerating voltage of ≈6kV or by fast atom bombardment (FAB) with a caesium ion gun and a MNOBA matrix with an addition of Na as required. Elemental analyses of compounds were preformed within UCL, by the microanalysis division. Gas Chromatography was performed on a Hewlett Packard 5890A with flame ionisation detection using an SPE 25 m X 0.32 mm BPx5 column. HPLC was performed on a Gilson system using a Phenomenex Luna C_{18} reverse phase column, with acetonitrile containing TFA (0.05%) as the mobile phase. Analysis was performed using a gradient with water as the second component, which began with 5% organic and finished at 95%.

All reagents and starting materials unless otherwise stated were bought from common chemical suppliers and purified as required according to established procedures.[452] Hydroxylamine-O-sulphonic acid was purified by precipitation from AcOH. A typical procedure was Hydroxylamine-O-sulphonic acid (5.65 g, 50.0 mmol) was dissolved in

H_2O (5.7 mL) and precipitated using acetic acid (40 mL, glacial). The pure product was dried between filter papers. KO^{t}Bu was sublimed before use and stored in the glove box for use in transfer hydrogenation reactions.

Na/Hg 2% w/w amalgam

The *title compound* was prepared by the slow addition of Na^0 (9.60 g, 0.42 mol, 1.0 eq) to a round bottom flask containing Hg^0 (370.00 g, 1.84 mol, 4.4 eq) at room temperature, with stirring provided by an overhead stirrer. The metallic grey liquid became solid on cooling and was used as required.

Na/K amalgam

The *title compound* was prepared by addition of K^0 (3.00 g, 76.7 mmol, 1.0 eq) to diethyl ether (~100 mL) followed by careful introduction of ~3 drops of water. To this, Na (0) (1.00 g, 43.5 mmol, 1.8 eq) was added and the two metals slowly brought in contact with each other using a glass rod and carefully ground together. This resulted in the formation of a metallic liquid. The ether was removed *via* cannula and the amalgam dried *in vacuo* and stored under inert conditions.

$TiCl_3(DME)_{1.5}$[453]

The *title compound* was prepared by a literature method.[453] $TiCl_3$ (0.87 g, 5.61 mmol) was suspended in DME (15.00 mL, 0.17 mol, 30.3 eq) and refluxed for 48 hours. On cooling, the reaction was filtered under nitrogen using a filter paper tipped cannula. The residual solid was washed with pentane (3 x 20 mL), and dried *in-vacuo* to give a fluffy, blue product (1.09 g, 3.76 mmol, 67%)

Zn-Cu couple[453]

The *title compound* was prepared by a literature method.[453] Zinc dust (4.90 g, 75.0 mmol, 31.9 eq) was added to deoxygenated (nitrogen-purged) water (20 mL), with further purging for 15 minutes, followed by an addition of $CuSO_4$ (0.38 g, 2.35 mmol, 1.0 eq). The black slurry was filtered under nitrogen using a filter paper tipped cannula,

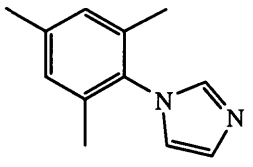
washed with deoxygenated water (10 mL x 2), acetone (10 mL x 2), and ether (10 mL x 2), and then dried *in-vacuo*.

Silver (I) oxide[454]

The *title compound* was prepared by a literature method.[454] An aqueous silver nitrate solution (9 mL, 1 M, 5.88 mmol, 1.0 eq) was added to an aqueous sodium hydroxide solution (9 mL, 1 M, 5.88 mmol, 1.0 eq) and stirred for 15 minutes at room temperature under ambient conditions. The precipitate was collected *via* filtration and washed successively with water (20 mL), acetone (20 mL), and ether (20 mL). The solid was dried *in-vacuo* to give the *title compound* as a grey powder.

Ligand and complex synthesis for transfer hydrogenation and oxidation studies.

1-(2,4,6-Trimethyl-phenyl)-1*H*-imidazole 96[455,456]

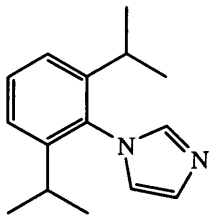


$C_{12}H_{14}N_2$
186.11570 g/mol

The *title compound* was prepared by a literature method.[455] Acetic acid (200 mL), formaldehyde (60.0 mL, 0.68 mol, 1.0 eq) and glyoxal (92.0 mL, 0.8 mol, 1.2 eq) were combined and heated to 70 °C. A mixture of acetic acid (200 mL), ammonium carbonate (62.0 g, 0.8 mol, 1.2 eq), water (20 mL) and 2,4,6-trimethylaniline (112.0 mL, 0.86 mol, 1.3 eq) was added over a 30-minute period, maintaining the temperature at 70 °C, followed by stirring for 12 hours. The dark brown reaction solution was cooled to room temperature and slowly added to a solution of water (6 dm^3) and sodium hydrogen carbonate (588.0 g) which resulted in significant effervescence and concomitant formation of a flocculent brown solid. The solution was filtered and the solid washed with water (3 x 300 mL). The brown solid was purified *via* a trap-to-trap distillation procedure using a Bunsen burner and high vacuum (0.1 torr) to yield a white solid (109.75 g, 0.59 mol, 75%). **Melting point** 111 – 113 °C, lit.[456] 112 – 113 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.98 (6H, s, *o*-C$\underline{H}_3$), 2.33 (3H, s, *p*-C$\underline{H}_3$), 6.87 (1H, dd, ^{4}J=1.2Hz, C$\underline{H}$ 4-imidazol-2-ylidene), 6.95 (2H, br s, ArC$\underline{H}$), 7.22 (1H, dd, ^{4}J=0.9Hz,

C*H* 5-imidazol-2-ylidene), 7.42(1H, d, ^{4}J=0.6Hz, C*H* 4-imidazol-2-ylidene) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 17.26 (*o*-$\underline{C}H_3$), 20.97 (*p*-$\underline{C}H_3$), 120.03 (4,5-imidazol-2-ylidene, $\underline{C}$H), 128.97 (Ar$\underline{C}$H), 129.48 (4,5-imidazol-2-ylidene $\underline{C}$H), 133.41 (Ar$\underline{C}$H), 135.40 (Ar$\underline{C}$H), 137.45 (Ar$\underline{C}_Q$), 138.81 (imidazol-2-ylidene $\underline{C}$H) **MS (EI)** *m/z* (%): 373 (35, 2xM+H$^+$), 186 (85, M$^+$) **FTIR (ν_{max} cm^{-1})** KBr 3445 (=NH, br), 3120 (s), 3100 (s), 2985 (s), 2955 (s), 2919 (s), 2865 (s), 1645 (s), 1604 (s), 1502 (br), 1249 (s), 1069 (s), 825 (s)

1-(2,6-Di*iso*propyl-phenyl)-1*H*-imidazole 97 [457,458]

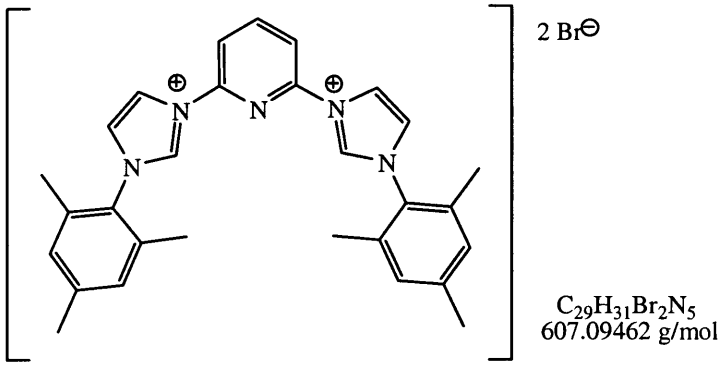


$C_{15}H_{20}N_2$
228.16265 g/mol

The *title compound* was prepared by a literature method.[457] Acetic acid (200.0 mL), formaldehyde (60.0 mL, 0.69 mol, 1.0 eq) and glyoxal (92.0 mL, 0.80 mol, 1.2 eq) were combined and heated to 70 °C. A mixture of acetic acid (200.0 mL), ammonium carbonate (62.0 g, 0.80 mol, 1.2 eq), water (20 mL) and 2,6-di*iso*propylaniline (112.0 mL, 0.86 mol, 1.3 eq) was added over a 30-minute period, maintaining the temperature at 70 °C, and left to stir for a further 12 hours. The dark red-brown reaction solution was cooled to room temperature and slowly added to a solution of water (6 dm^3) and sodium hydrogen carbonate (588.0 g) which resulted in significant effervescence and the concomitant formation of a flocculent brown solid. The solution was filtered and the solid washed with water (3 x 300 mL). The brown solid was purified *via* a trap-to-trap distillation procedure using a Bunsen burner and high vacuum (0.1 torr) to yield a white solid (100.87 g, 0.44 mol, 64%). **Melting point** 123 – 124 °C, lit.[458] 123 – 125 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ1.12 (12H, d, ^{3}J=7.0 Hz, ($C\underline{H}_3$)$_2$CH), 2.41 (2H, sep, ^{3}J=6.8Hz, C$\underline{H}$(CH$_3$)$_2$), 6.94 (1H, m, C$\underline{H}$ 4,5-imidazol-2-ylidene), 7.24 (1H, m, C$\underline{H}$ 4,5-imidazol-2-ylidene), 7.26 (2H, d, ^{3}J=7.8Hz, ArC$\underline{H}$), 7.43 (1H, m., C$\underline{H}$ imidazol-2-ylidene) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 24.36 (($\underline{C}H_3$)$_2$CH), 28.06 ($\underline{C}$H(CH_3)$_2$), 121.50 (4,5-imidazol-2-ylidene $\underline{C}$H), 123.70 (4,5-imidazol-2-ylidene $\underline{C}$H), 129.30 (Ar$\underline{C}$H), 129.75 (Ar$\underline{C}$H), 132.83 (Ar$\underline{C}_Q$(CH(CH_3)$_2$)), 138.44 (-N$^+$=$\underline{C}$H-N-), 146.51 (Ar$\underline{C}_Q$N) **MS**

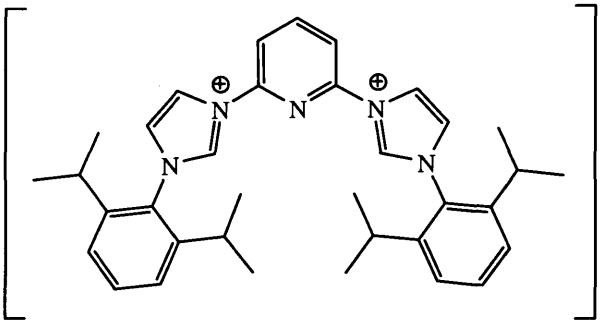
(EI) *m/z* (%): 228 (64, M^+), 201 (60), 186 (100, M-C_3H_7) **FTIR** (ν_{max} **cm^{-1}**) KBr 3450 (=NH, br), 3048 (br), 3018 (br), 2942 (s), 1623 (s), 1616 (s), 1491 (br), 1324 (s), 1053 (s), 769 (s)

2,6-bis- [3-(2,4,6 trimethylphenyl)-imidazolium]-pyridine dibromide 98



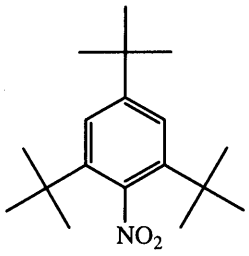
The *title compound* was synthesised by the addition of mesityl imidazole **96** (3.0 g, 16.13 mmol, 2.0 eq) to 2,6-dibromopyridine (1.91 g, 8.07 mmol, 1.0 eq) in a glass ampoule, which was evacuated and sealed, prior to placing in an oven at 160 °C for four days. After cooling, the dark solid was removed from the ampoule and stirred vigorously with ether, before being filtered and dried *in-vacuo* to give the *title compound* as a cream coloured powder (3.63 g, 5.98 mmol, 74%) **Melting point** 219 – 220 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.18(12H, s, *o*-C*H*$_3$), 2.32(6H, s, *p*-C*H*$_3$), 7.01 (4H, s, ArC*H*), 7.34 (2H, d ^{3}J=1.8Hz), pyridine 3 & 5-C*H*), 8.29 (1H, t, J=8.1Hz, pyridine 4-C*H*), 9.11 (2H, d, ^{3}J=8.2Hz, C*H* 4-imidazol-2-ylidene), 9.86 (2H, m, 5-imidazol-2-ylidene C*H*), 11.90 (2H, d, ^{4}J=1.3Hz, imidazol-2-ylidene) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 15.52 (*o*-Ar*C*H$_3$), 20.50 (*p*-Ar*C*H$_3$), 112.07 (Pyridine 3 & 5-*C*H), 112.41, 123.81 (Ar*C*H), 131.89 (*o*-ArC_Q), 135.06 (Ar*C*H), 136.56 (Ar*C*H), 138.68 (Ar*C*$_Q$), 141.82 (Ar*C*H), 143.36 (Ar*C*H), 161.22 (Ar*C*H) **HRMS (ES)** *m/z* (%):$[C_{29}H_{31}N_5]^{2+}$ requires 224.62842, found 224.62755 **MS (FAB) (MNOBA)** *m/z* (%): 448 (100, M-2xBr), 263 (61, M-2xBr-1($C_{12}N_2H_{14}$)), 187 (15, mesityl imidazole) **FTIR** (ν_{max} **cm^{-1}**) KBr 3425 (br), 3040 (s), 2970 (s), 2930 (s), 2875 (s), 1619 (s), 1529 (s), 1464 (s), 1229 (s) 814 (s) **Elemental analysis** calculated C 57.16%, H 5.13%, N 11.49%; Found C 57.22%, H 5.19%, N 11.38%

2,6-bis-[3-(2,6-di*iso*propylphenyl)-imidazolium]-pyridine dibromide 99



The *title compound* was synthesised by the addition of 2,6-di*iso*propyl imidazole **97** (3.0 g, 13.14 mmol, 2.0 eq) to 2,6-dibromopyridine (1.56 g, 8.07 mmol, 1.0 eq) in a glass ampoule, which was evacuated and sealed, prior to placing in an oven at 160 °C for four days. After cooling, the dark solid was removed from the ampoule and stirred vigorously with ether before being filtered and dried *in-vacuo* to give the *title compound* as a cream coloured powder (7.08 g, 10.25 mmol, 78% yield). **Melting point** >220 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.15 (12H, d, ^{3}J=6.9Hz, $(C\underline{H}_3)_2CH$), 1.27 (12H, d ^{3}J =6.8Hz, $(C\underline{H}_3)_2CH$), 2.45 (4H, sep ^{3}J=6.9Hz, $(C\underline{H}(CH_3)_2)$, 7.30 (4H, d, ^{3}J=7.9Hz ArC*H*), 7.36 (2H, m, 4-imidazol-2-ylidene C*H*), 7.53 (2H, dd, ^{3}J=7.8Hz, *p*-ArC*H*), 8.34 (1H, d, ^{3}J=8.2Hz, pyridine *p*-C*H*), 9.15 (2H, d, ^{3}J=8.2Hz, pyridine 3 & 5-C*H*), 9.95 (2H, m, 5-imidazol-2-ylidene), 12.09 (2H, m, imidazol-2-ylidene) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 24.11 $(\underline{C}H_3)_2CH$), 24.53 $(\underline{C}H_3)_2CH$), 27.27 $((CH_3)_2\underline{C}H)$, 110.56 (Ar*C*H), 112.07 (Ar*C*H), 123.81 (Ar*C*H), 125.34 (Ar*C*H), 127.99 ($Ar\underline{C}_Q$), 135.68 (Ar*C*H), 141.82 (Ar*C*H), 143.36 (ArCH), 145.80 (ArCH), 161.60 (ArCH) **HRMS (ES)** *m/z* (%):$[C_{35}H_{43}N_5]^{2+}$ Requires 266.67537; Found 266.67518 **MS (FAB) (MNOBA + Na)** *m/z* (%): 532 (100, M-2xBr), 305 (65, (M-(2xBr+($C_{15}N_2H_{20}$)), 229 (10, 2,6 diisopropyl phenylimidazole) **FTIR (ν_{max} cm^{-1})** KBr 3430 (br), 3055 (br), 3025 (br), 2965 (s), 1614 (s), 1534 (s), 1459 (s), 1239 (s), 1059 (s), 819 (s), 679 (w) **Elemental analysis** calculated C 60.61%, H 6.25%, N 10.10%; Found C 60.99%, H 6.37%, N 9.68%

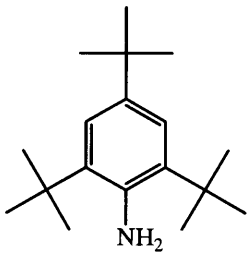
2,4,6-Tris-*tert*-butyl-1-nitro-benzene 101[459,460]



$C_{18}H_{29}NO_2$
291.21983 g/mol

The *title compound* was prepared by a literature method.[459] 1,3,5-tris-*tert*-butylbenzene (4.4 g, 17.86 mmol, 1.0 eq) was slurried in acetic anhydride (15 mL) and cooled to 0 °C. A solution of fuming nitric acid (1.13 mL, 26.85 mmol, 1.5 eq), acetic acid (1.02 mL, 19.90 mmol, 1.0 eq) and acetic anhydride (2.96 mL, 31.33 mmol, 1.75 eq) was added to the cooled slurry over 15 minutes. The reaction was allowed to warm to room temperature and stirred for a further 4 hours before being poured onto ice. The yellow needles were collected *via* filtration and recrystallised from methanol to yield cream coloured needles (3.95 g, 13.56 mmol, 75%). **Melting point** 205 - 207 °C, lit.[460] 205 – 206 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.31 (9H, s, ArC(C$\underline{H}_3$)$_3$), 1.37 (18H, s, ArC(C$\underline{H}_3$)$_3$), 7.43 (2H, s, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 31.25 (-C($\underline{C}$H$_3$)$_3$), 35.18 (*p*-C($\underline{C}$H$_3$)$_3$), 36.32 (*o*-ArC($\underline{C}$H$_3$)$_3$), 123.52 (Ar$\underline{C}$H), 140.12 (*o*-Ar$\underline{C}_Q$), 147.03 (Ar$\underline{C}_Q$NO$_2$), 151.33 (*p*-ArC($\underline{C}$H$_3$)$_3$) **MS (EI)** *m/z* (%): 291 (80, M^+), 277 (95, M-CH_3+H) **FTIR (ν_{max} cm^{-1})** KBr 2965 (s), 2915 (s), 2880 (s), 1609 (w), 1474 (s), 1374 (s), 1224 (s), 849 (w)

2,4,6-Tris-*tert*-butylaniline 102[459,460]

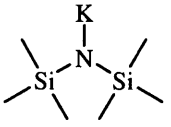


$C_{18}H_{31}N$
261.24565 g/mol

The *title compound* was prepared by a literature method.[459] 2,4,6-tris-*tert*-butylnitrobenzene **101** (4.10 g, 14.02 mmol) was added to methanol (100 mL) to form a slurry. Na/Hg 2% w/w amalgam (1.50 g) was added and the reaction heated to reflux

for 8 hours. The solution was cooled to room temperature and the solid was collected *via* filtration. Recrystallisation from methanol gave the *title compound* as white needles (3.10 g, 11.87 mmol, 84%). **Melting point** 147 °C, lit.[460] 147 - 148 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ1.34 (9H, s, *p*-ArC($C\underline{H}_3$)$_3$), 1.51 (18H s, *o*-ArC($C\underline{H}_3$)$_3$), 4.07 (2H, br s, $N\underline{H}_2$), 7.28 (2H, s, Ar$C\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 30.39 (*o*-ArC($\underline{C}H_3$)$_3$), 31.73 (*o*-ArC($\underline{C}H_3$)$_3$), 34.44 (*p*-$\underline{C}_Q$(CH_3)$_3$), 34.81 (*o*-$\underline{C}_Q$(CH_3)$_3$), 121.90 (Ar$\underline{C}$H), 133.52 (*p*-Ar$\underline{C}_Q$C($\underline{C}H_3$)$_3$), 139.10 (*o*-Ar$\underline{C}_Q$C($\underline{C}H_3$)$_3$), 141.11(Ar$\underline{C}_Q$$NH_2$) **HRMS (EI)** *m/z* (%): ($C_{18}H_{31}N$) Requires 261.24564; Found 261.16921 (100, M^+), 245 (80, M-NH_3), 57 (65, C_4H_9) **FTIR (ν_{max} cm^{-1})** KBr 3430 (NH, br), 2965 (s), 2915 (s), 2875 (s), 1599 (w), 1379 (s), 1219 (s), 849 (w)

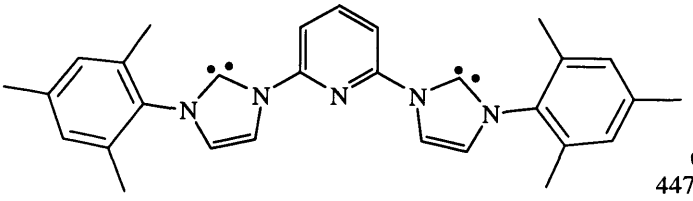
Potassium hexamethyldisilazide 104



$C_6H_{18}KNSi_2$
199.06148 g/mol

The *title compound* was prepared by adding KH (2.64 g, 66.0 mmol, 1.0 eq) to a solution of $HN(TMS)_2$ (13.76 mL, 66.0 mmol, 1.0 eq) in toluene (50 mL). The reaction was heated to reflux for 5 hours, before being cooled to room temperature and the volatiles removed *in-vacuo* to give the *title compound* as a white solid (13.13 g, 66.0 mmol, 100%) **^{1}HNMR** (C_6D_6, 300MHz): δ 0.07 (18H, s, $C\underline{H}_3$) **^{13}CNMR** (C_6D_6, 75.5MHz): δ 1.90 ($\underline{C}H_3$)

2,6-bis-[3-(2,4,6 trimethylphenyl)phenylimidazolylidene]pyridine 105

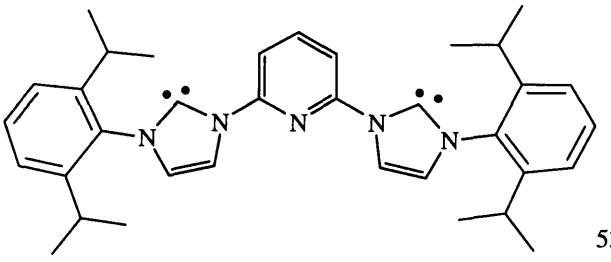


$C_{29}H_{29}N_5$
447.24240g/mol

The *title compound* was synthesised by the combination of 2,6-bis- [3-(2,4,6 trimethylphenyl)-imidazolium]-pyridine dibromide **98** (5.0 g, 8.22 mmol, 1.0 eq) that, immediately prior to use was azeotropically dried in toluene, and $KN(TMS)_2$ **104**

(3.27g, 16.4mM, 2 eq). The combined solids were cooled to -78 °C and THF (200 mL, -78 °C), was added. The reaction mixture was allowed warm to room temperature and then stirred for 4 hours. The volatiles were removed *in vacuo* and the resulting solid extracted into benzene (2 x 75 mL), which was filtered through celite, under N_2. The filtrate was concentrated to dryness *in-vacuo* to give the *title compound* as a cream coloured solid (2.52 g, 5.63 mmol, 68%). The sensitivity of this compound precluded full structural characterisation. **^{1}HNMR** (C_6D_6, 500MHz): δ 2.11 (12H, s, *o*-ArC$\underline{H}_3$), 2.13 (6H, s, *p*-ArC$\underline{H}_3$), 6.45 (2H, d ^{3}J=1.4Hz, C$\underline{H}$ 4-imidazol-2-ylidene), 6.79 (4H, s, ArC$\underline{H}$), 7.10 (1H, dd, ^{3}J=8.0Hz, pyridine *p*-C$\underline{H}$), 7.14 (4H, s, ArC$\underline{H}$), 8.10 (2H, d J=1.4Hz, C$\underline{H}$ 5-imidazol-2-ylidene), 8.52 (2H, d ^{3}J=8.0Hz, pyridine *m*-C$\underline{H}$) **^{13}CNMR** (C_6D_6, 125.75MHz): δ 18.02 (*o*-Ar$\underline{C}$H$_3$), 20.97 (*p*-Ar$\underline{C}$H$_3$), 111.49 (pyridine *m*-$\underline{C}$H), 116.48 (Ar$\underline{C}$H), 121.44 (Ar$\underline{C}$H), 129.17 (pyridine *p*-$\underline{C}$H), 135.27 (*o*-Ar$\underline{C}_Q$CH$_3$), 137.60 (ArC_QN-), 138.89 (*p*-Ar$\underline{C}_Q$CH$_3$), 140.67 (Ar$\underline{C}$H), 152.67 (pyridine$\underline{C}_Q$), 219.73 (carbene $\underline{C}_Q$)

2,6-bis-[3-(2,6-di*iso*propyl)phenylimidazolylidene]pyridine 106

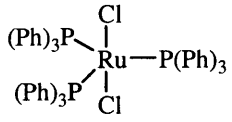


$C_{29}H_{29}N_5$
535.33638 g/mol

The *title compound* was synthesised by the combination of 2,6-bis-[3-(2,6-di*iso*propyl)-imidazolium]-pyridine dibromide **99** (3.0 g, 4.3 mmol, 1.0 eq) that, immediately prior to use was azeotropically dried in toluene, and KN(TMS)$_2$ **104**(1.74 g, 8.7 mmol, 2.0 eq). The combined solids were cooled to -78 °C and THF (100 mL, -78 °C), added. The reaction mixture was allowed warm to room temperature and then stirred for 4 hours. The volatiles were removed *in vacuo* and the resulting solid extracted into benzene (2 x 50 mL) and filtered through celite, under N_2. The filtrate was concentrated to dryness *in-vacuo* to give the *title compound* as a cream coloured solid (1.64 g, 3.06 mmol, 70%). The instability of this compound precluded full structural characterisation. **^{1}HNMR** (C_6D_6, 500MHz): δ 1.09 (12H, d, ^{3}J=7.2Hz CH(C$\underline{H}_3$)$_2$), 1.18 (12H, d, J=6.7Hz, CH(C$\underline{H}_3$)$_2$), 2.90 (4H, sep, ^{3}J=6.7Hz (C$\underline{H}$(^{i}Pr CH$_3$)$_2$)), 6.62 (2H, d, ^{3}J=1.4Hz, 4-

imidazol-2-ylidene C<u>H</u>), 7.06 (1H, t, ^{3}J=8.0Hz pyridine *p*-C<u>H</u>), 7.13 (4H, d, ^{3}J=7.8Hz, *m*-ArC<u>H</u>), 7.26 (2H, dd, ^{3}J=7.2Hz, Ar *p*-C<u>H</u>), 8.06 (2H, d, J=1.9, 5-imidazol-2-ylidene C<u>H</u>), 8.43 (2H, d, ^{3}J=7.6, pyridine *m*-C<u>H</u>) **^{13}CNMR** (C_6D_6, 125.75MHz): δ 24.01 (CH(<u>C</u>H$_3$)$_2$), 24.40 (CH(<u>C</u>H$_3$)$_2$), 28.58 (<u>C</u>H(CH$_3$)$_2$), 111.68 (pyridine *m*-<u>C</u>H), 116.24, 122.81, 123.78, 129.24 (pyridine *p*-<u>C</u>H), 138.70 (Ar<u>C</u>$_Q$N-), 140.68 (Ar<u>C</u>$_Q$C), 146.18, 152.61 (pyridine <u>C</u>$_Q$), 220.38 (carbene <u>C</u>$_Q$) **X-ray** see appendix

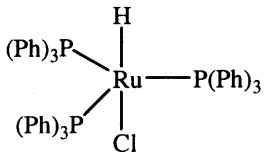
Ruthenium dichloride tris triphenylphosphine 107[461]



$C_{54}H_{45}Cl_2P_3Ru$
958.11546 g/mol

The *title compound* was prepared by a literature method.[461] $RuCl_3.3H_2O$ (1.00 g, 3.8 mmol, 1.0 eq) was dissolved in methanol (250 mL), anti-bumping granules were added and the solution refluxed for 15 minutes, using a heating mantle. The solution was cooled to room temperature and triphenyl phosphine, (6.00 g, 22.9 mmol, 6.0 eq) added. The reaction solution was then returned to reflux for 4 hours. A shiny black crystalline precipitate formed over time. The solution was cooled to room temperature and filtered under N_2 using a filter tipped cannula, and the collected solid was washed with diethyl ether (3 x 50 mL), and petroleum spirit (3 x 50 mL), before being dried *in-vacuo* to provide shiny, free flowing, black crystals (2.96 g, 3.08 mmol, 81%). **Melting point** 133 - 134 °C, lit.[461] 132- 134 °C **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 6.96 (18H, dd ^{3}J=7.6Hz, ArC<u>H</u>), 7.21 (28H, m, ArC<u>H</u>) **^{13}CNMR** (CD_2Cl_2, 125.75MHz): δ127.43 (Ar<u>C</u>H), 129.48 (Ar<u>C</u>H), 134.89 (Ar<u>C</u>$_Q$), 135.24 (Ar<u>C</u>H) **^{31}PNMR** (CD_2Cl_2, 202.50MHz): δ 41.99 (broad peak, bound PPh_3)

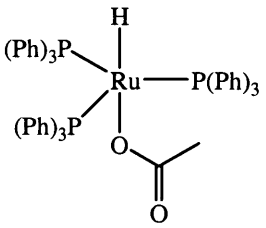
Hydridochlorotris(tripheny1phosphine)ruthenium 108[462]



$C_{54}H_{46}ClP_3Ru$
924.15444g/mol

The *title compound* was prepared by a literature method.[462] To a solution of $RuCl_2(PPh_3)_3$ C$XX (1.0 g, 1.08 mmol, 1.0 eq) in benzene (125 mL), sodium borohydride (210 mg, 5.5 mmol, 5.0 eq) in water (2 mL) was added. The reaction was heated to reflux and N_2 was bubbled through the solution, which developed a red-violet colour within 25 minutes. After 2 hours under reflux, the solution was cooled to room temperature, filtered under N_2 using a filter tipped cannula to remove sodium chloride, and the volatiles reduced *in-vacuo* by *circa* 75%, at which point black crystals precipitated from the solution. These were collected by removal of the reaction solvent *via* a filter tipped cannula and washed with diethyl ether (5 mL x 3) to give the *title compound* (0.79 mmol, 0.73 g, 73%) **Melting point** 215 °C, lit.[462] 218 – 220 °C **^{1}HNMR** (C_6D_6, 500MHz): δ -17.55 (1H, q, $^{P-H}$J=25.8Hz) 6.91 (7H, dd, ^{3}J=7.5, 7.7Hz, ArC*H*), 7.01 (5H, dd, ^{3}J=7.2, 7.3Hz, ArC*H*), 7.04-7.11 (10H, m, ArC*H*), 7.11-7.14 (7H, m, ArC*H*), 7.63 (5H, dd, ^{3}J=8.0, 8.4Hz, ArC*H*), 7.80-7.87 (10H, m, ArC*H*) **^{13}CNMR** (C_6D_6, 125.75MHz): δ127.43 (ArCH), 129.48 (ArCH), 134.89 (ArC_Q), 135.24 (ArCH) **^{31}PNMR** (C_6D_6, 202.50MHz): δ 29.04 ($PO(Ph)_3$) 59.01 (bound PPh_3)

Hydridoacetatotris(tripheny1phosphine)ruthenium 109[463]

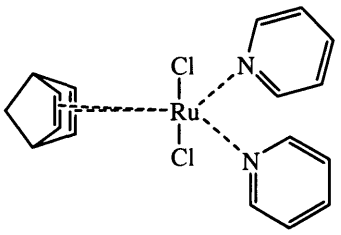


$C_{56}H_{49}O_2P_3Ru$
948.19889 g/mol

The *title compound* was prepared by a literature method.[463] $RuCl_3.3H_2O$ (0.50 g, 1.9 mmol, 1.0 eq), triphenyl phosphine (3.00 g, 11.5 mmol, 6.0 eq) and $NaOAc.3H_20$ (2.60 g, 19.1mmol, 10.0 eq) were dissolved in methanol (85 mL), anti-bumping granules were added and the reaction solution was heated to reflux for 5 hours using a heating mantle.

The reaction was filtered whilst hot to collect the yellow complex that precipitated during the reaction. The solid was washed with ethanol (25 mL), water (25 mL) and ethanol (25 mL) and dried *in-vacuo* over silica gel, which gave the product as a yellow crystalline material (0.98 g, 1.03 mmol, 54%). The instability of this compound precluded the recoding of its melting point. **^{1}HNMR** (C_6D_6, 500MHz): δ -19.87 (1H, quart, $^{P\text{-}H}$J=26.1Hz, Ru-H), 1.52 (3H, s, C*H*$_3$CORu), 7.05 (27H, m, ArC*H*), 7.59 (27H, m, ArC*H*) **^{13}CNMR** (C_6D_6, 125.75MHz): 23.40 (*C*H$_3$CORu), 127.71 (t, $^{P\text{-}C}$J=3.8Hz Ar*C*H), 128.29 (Ar*C*$_Q$), 129.98 (Ar*C*$_Q$), 134.87 (t, $^{P\text{-}C}$J=6.8Hz Ar*C*H), 188.75 (*C*$_Q$O) **^{31}PNMR** (C_6D_6, 202.50MHz): δ 78.72 (bound PPh_3)

***trans*-Ru(Cl)$_2$(NBD)(Py)$_2$ 110**[464,465]

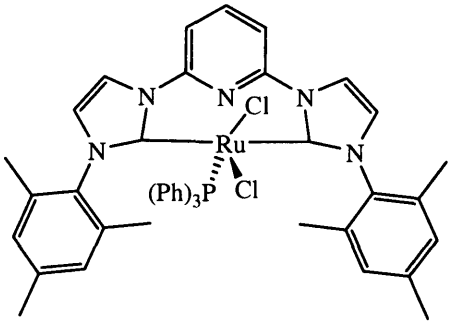


$C_{19}H_{24}Cl_2N_2Ru$
452.03600 g/mol

The *title compound* was prepared by a combination of literature methods.[464,465] Initially 1/n (Norbornadiene-$RuCl_2$)$_n$ was prepared following a modified literature procedure.[464] $RuCl_3.3H_2O$ (0.80 g, 3.06 mmol, 1.0 eq) was dissolved in ethanol (60 mL, 96%) and anti-bumping granules were added, followed by freshly distilled norbornadiene (1.92 mL, 24.48 mmol, 8.0 eq). The reaction was heated to reflux using a heating mantle and maintained at this temperature for 60 hours. The solution developed an orange colouration and a brown/orange solid precipitated from the solution. The reaction was cooled to room temperature, filtered and the solid washed with ethanol (20 mL x 2, 96%). The insoluble polymer was dried *in-vacuo* to yield *1/n (Norbornadiene-$RuCl_2$)$_n$* (0.71 g, 2.65 mmol, 87%). $RuCl_2$(NBD)(pip)$_2$ was synthesised following a literature method.[465] 1/n (Norbornadiene-$RuCl_2$)$_n$ (0.71 g, 2.65 mmol, 1.0 eq) and piperidine (1.30 mL, 13.36 mmol, 5.0 eq) were dissolved in acetone (3.0 mL) and stirred at room temperature for 16 hours. Petroleum spirit (42 mL) was added to complete the precipitation of the light brown/yellow material from the dark reaction mixture. The reaction was filtered, the solid washed with petroleum spirit (40 mL), and dried *in-vacuo* to give *trans-$RuCl_2$(NBD)(pip)$_2$* as a brown/yellow solid (0.52g, 1.21mM, 46%).

trans-$RuCl_2(NBD)(pip)_2$ (0.52g, 1.21mM, 1.0 eq) was dissolved in DCM (5 mL) and stirred with pyridine (18.60 mL, 217.00 mM, 180.0 eq) at room temperature for 3 hours. The product was precipitated by the addition of petroleum spirit (500 mL) to the yellow reaction solution. Recrystallisation of the precipitate from DCM/petroleum spirit provided the *title compound* as yellow/orange powder that was dried *in-vacuo* (385mg, 0.85 mmol, 70%) **Melting Point** 218 °C (decomp.) lit. value not given **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 1.55 (2H, br s, C*H*$_2$), 4.06 (2H, br s, C*H*), 4.82 (4H, m, C*H*=C*H*), 7.23 (4H, t, ^{3}J=11.9Hz, ArC*H*), 7.68 (2H, t, ^{3}J=11.9Hz, ArC*H*), 8.52 (4H, d, ^{3}J=12.0Hz, ArC*H*) **^{13}CNMR** (CD_2Cl_2, 125.75MHz): δ 49.31 (*C*H$_2$), 62.24 (*C*H), 73.72 (H*C*=*C*H), 125.84 (Ar*C*H), 126.21 (Ar*C*H), 139.11 (Ar*C*H), 135.24 (Ar*C*H)

2,6-bis-[3-(2,4,6 trimethylphenyl)phenylimidazolylidene]pyridine ruthenium dichloride triphenylphosphine complex 111

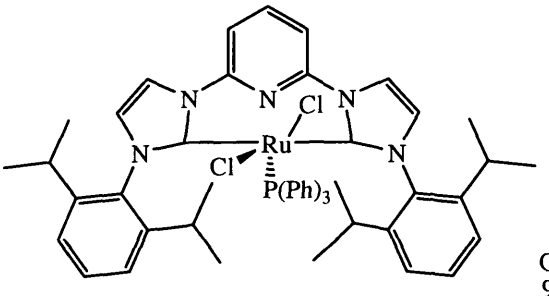


$C_{47}H_{44}Cl_2N_5PRu$
881.17549 g/mol

The *title compound* was synthesised by the addition of a $RuCl_2(PPh_3)_3$ **107** (3.26 g, 3.4 mmol, 1.0 eq) slurry in THF (150 mL), at –78 °C, to a solution of 2,6-bis-[3-(2,4,6 trimethylphenyl)phenylimidazolylidene]pyridine **105** (1.52 g, 3.4 mmol, 1.0 eq) in THF (100 mL), at –78 °C, *via* cannula. The suspension was allowed warm to room temperature and stirred for a further 4 hours. The reaction developed a red precipitate as the complex was formed. The volatiles were removed *in vacuo*, and the solid was washed with diethyl ether (25 mL x 4) and petroleum spirit (25 mL) before drying *in vacuo* to give an orange solid (1.20 g, 1.36 mmol, 40%). **Melting Point** 202 °C (decomp.) **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 0.94 (6H, s, ArC*H*$_3$), 2.31 (6H, s, ArC*H*$_3$), 2.69 (6H, s, ArC*H*$_3$), 6.59 (2H, m, 4-imidazol-2-ylidene C*H*), 6.7 – 7.23 (24H, m., triphenyl phosphine (15), Mesityl (4), Pyridine (3), ArC*H*, 5-imidazol-2-ylidene (2)) **^{13}CNMR** (CD_2Cl_2, 125.75MHz): δ 17.24 (Ar*C*H$_3$), 20.58 (Ar*C*H$_3$) 21.07 (Ar*C*H$_3$), 43.73, 113.92, 126.32, 127.87, 129.00, 131.24, 131.36, 134.71, 135.38, 137.57, 138.35

(aromatic, pyridine and carbene ring carbons) carbene carbon not observed **^{31}PNMR** (CD_2Cl_2, 202.50MHz): δ –4.37 (Free PPh_3), 48.15 (bound PPh_3) **HRMS FAB** *m/z* (%): ($C_{47}H_{44}Cl_2N_5PRu$, M+H-Cl) Requires 847.21443, Found 847.21774 (100, M+H-Cl), 544 (80), 280 (95) **FTIR (ν_{max} cm^{-1})** KBr 3204 (br), 3121 (s), 2956 (w), 1612 (s), 1486 (s), 1455 (s), 1401 (s), 1283 (s), 1168 (s), 1126 (s), 1079 (s), 914 (s), 835 (s), 899 (s) **X-Ray** see appendix

2,6-bis-[3-(2,6-di*iso*propyl)phenylimidazolylidene]pyridine ruthenium dichloride triphenylphosphine complex 112

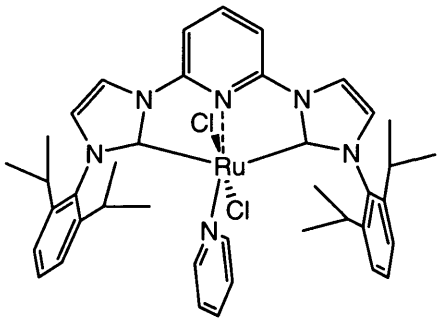


$C_{53}H_{56}Cl_2N_5PRu$
965.26939 g/mol

The *title compound* was synthesised by the addition of a $RuCl_2(PPh_3)_3$ **107** (3.26 g, 3.4 mmol, 1.0 eq) slurry, in THF (150 mL), at –78 °C, to a solution of 2,6-bis-[3-(2,6-di*iso*propyl)phenylimidazolylidene]pyridine **106** (1.82 g, 3.4 mmol, 1.0 eq) in THF (100 mL) at –78 °C, *via* cannula. The suspension was allowed warm to room temperature and stirred for a further 4 hours. The reaction developed a red precipitate as the complex was formed. The volatiles were removed *in vacuo*, the solid was washed with diethyl ether (25 mL x 4) and petroleum spirit (25 mL) before being dried *in vacuo* to give an orange solid (1.05 g, 1.09 mmol, 28%). **Melting Point** 211 °C (decomp.) **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 0.88 (3H, d, ^{3}J=6.6Hz, C$\underline{H}_3$), 0.55 (3H, d, ^{3}J=6.6Hz, C$\underline{H}_3$), 0.72 (3H, d, ^{3}J=7.0Hz, C$\underline{H}_3$), 0.81 (3H, d, ^{3}J=6.9Hz, C$\underline{H}_3$), 0.84 (3H, d, ^{3}J=6.6Hz, C$\underline{H}_3$), 0.87 (3H, d, ^{3}J=6.9Hz, C$\underline{H}_3$), 1.08 (3H, d, ^{3}J=6.4Hz, C$\underline{H}_3$), 1.11 (3H, d, ^{3}J=6.4Hz, C$\underline{H}_3$), 2.25 (1H sep, ^{3}J=6.6Hz, C$\underline{H}$(CH$_3$)$_2$), 2.32 (1H sep, J=7.1Hz, C$\underline{H}$(CH$_3$)$_2$), 3.15 (1H sep, ^{3}J=6.6Hz, C$\underline{H}$(CH$_3$)$_2$), 3.42 (1H sep, ^{3}J=6.6Hz, C$\underline{H}$(CH$_3$)$_2$) 6.65 – 8.64 (28H, m, ArC$\underline{H}$, PPh_3 (15H), Di-^{i}PrAr (6H), py (3H), Imid (4H)) **^{13}CNMR** (CD_2Cl_2, 125.75MHz): δ 22.53 (C$\underline{H}_3$), 22.65 (C$\underline{H}_3$), 23.14 (C$\underline{H}_3$), 25.65 (C$\underline{H}_3$), 25.94 (C$\underline{H}_3$), 28.47 (C$\underline{H}$(CH$_3$)$_2$), 116.33, 116.56, 122.87, 123.46, 124.83, 127.29, 128.57, 130.17, 133.66, 133.81 (aromatic, pyridine and carbene ring carbons), carbene carbon not

observed ^{31}**PNMR** (CD_2Cl_2, 202.50MHz): δ –4.37 (Free PPh_3), 39.86 (bound PPh_3) **HRMS FAB** *m/z* (%): ($C_{53}H_{56}ClN_5PRu$ M+H-Cl) Requires 932.31619, Found 932.31587 (100, M+H-Cl), 442 (60), 319 (90) **FTIR** (ν_{max} **cm^{-1}**) KBr 3210 (br), 3118 (s), 2941 (w), 2901 (w), 1608 (s), 1491 (s), 1454 (s), 1417 (s), 1287 (s), 1174 (s), 1121 (s), 1082 (s), 925 (s), 821 (s), 880 (s), 748 (s), 680 (s) **X-Ray** see appendix

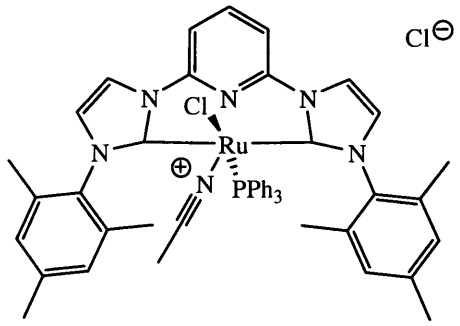
2,6-bis-[3-(2,6-di*iso*propyl)phenylimidazolylidene]pyridine ruthenium dichloride pyridine complex 113



$C_{40}H_{46}Cl_2N_6Ru$
782.22045 g/mol

The *title compound* was synthesised by the addition of *trans*-$Ru(Cl)_2(NBD)(Py)_2$ **110** (385mg, 0.85 mmol 1.0 eq) in THF (5 mL) at –78 °C, to a solution of 2,6-bis-[3-(2,6-di*iso*propyl)phenylimidazolylidene]pyridine **106** (455 mg, 0.85 mmol, 1.0 eq) in THF (5 mL), at –78 °C, *via* cannula. The suspension was allowed warm to room temperature with further stirring for 4 hours. The reaction developed a red precipitate as the complex was formed. The volatiles were removed *in vacuo*, and the solid was washed with diethyl ether (1 mL x 2) and petroleum spirit (1 mL) before being dried *in vacuo* to give an orange solid (78 mg, 0.10 mmol, 12%). This compound was unambiguously characterised by X-Ray (see appendix). No further characterisation was performed since the supply of material was limited and the only requirement was to study its solid-state conformation *via* X-Ray.

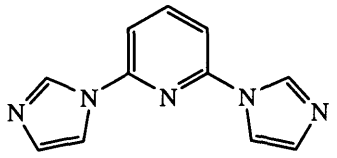
2,6-bis-[3-(2,4,6 trimethylphenyl)phenylimidazolylidene]pyridine ruthenium (II)$^+$ monochloro triphenylphosphine acetonitrile chloride complex 114



$C_{49}H_{47}Cl_2N_6PRu$
922.20204 g/mol

The *title compound* was synthesised by dissolution of 2,6-bis-[3-(2,4,6 trimethylphenyl) phenylimidazolylidene]pyridine-rutheniumdichloride triphenylphosphine complex, **111**, (100 mg, 0.11 mmol, 1.0 eq) in acetonitrile (1 mL) at room temperature. Slow evaporation of the solvent over ~24 hours resulted in yellow block shaped crystals of the product precipitating from the solution (98 mg, 0.11 mmol, 98%) **Melting Point** >220 °C **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 1.04 (6H, s, ArC$\underline{H}_3$), 1.18 (3H, s, C$\underline{H}_3$CN), 2.28 (6H, s, ArC$\underline{H}_3$), 2.32 (6H, s, ArC$\underline{H}_3$), 6.73 (8H, m), 6.94 (10H, m), 7.10 (3H, dt, ^{3}J=7.6Hz, ^{4}J=1.5Hz), 8.14 (3H, m), 8.56 (2H, d, J=2.0Hz) **^{13}CNMR** (CD_2Cl_2, 125.75MHz): δ 2.81 ($\underline{C}H_3CN$), 16.48 (Ar$\underline{C}H_3$), 190.58 (Ar$\underline{C}H_3$) 20.78 (Ar$\underline{C}H_3$), 108.04, 118.16, 125.84, 127.86, 128.32, 128.42, 128.74, 128.94, 129.29, 131.68, 131.78, 135.06, 135.32, 136.84, 137.29, 137.61, 139.15, 155.54, 195.32, 225.58 (aromatic, pyridine, nitrile and imidazolidine ring carbons) **^{31}PNMR** (CD_2Cl_2, 202.50MHz): δ – 4.37 (Free PPh_3), 46.82 (bound PPh_3) **HRMS FAB** *m/z* (%): ($C_{49}H_{47}ClN_6PRu$, M-Cl+H) Requires 888.24098, Found: 888.24273 (20, M-Cl+H), 846 (100), 544 (65) **FTIR (ν_{max} cm^{-1})** KBr 3420 (br), 3055 (w), 2920 (w), 2360 (w), 1619 (s), 1484 (s), 1409 (s), 1269 (s), 1099 (s), 924 (w), 699 (s) **X-Ray** see appendix

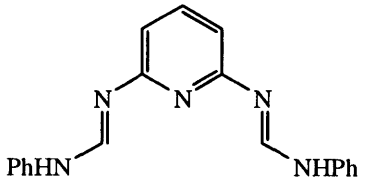
2,6-Di-imidazol-1-yl-pyridine 118[466]



$C_{11}H_9N_5$
211.08580 g/mol

The *title compound* was prepared by a modified literature method.[466] Imidazole (1.00 g, 14.7 mmol, 2.0 eq) and 2,6-dibromopyridine (1.74 g, 7.4 mmol, 1.0 eq) were added to a glass ampoule, which was evacuated and sealed, prior to placing in an oven at 100 °C for 60 hours. After cooling to room temperature, the dark solid was dissolved in $CHCl_3$ (25 mL), washed with water (3 x 20 mL) and brine (20 mL). The solution was dried, the volatiles were removed *in-vacuo* and the solid recrystallised from ethyl acetate, to give the *title compound* as a white powder (1.3 g, 6.1 mmol, 82% yield). **Melting point** 151 °C, lit.[466] 152 °C **^{1}HNMR** ($CDCl_3$-D_6, 300MHz): δ 7.23 (2H, t, ^{3}J=1.4Hz, 4-imidazol-2-ylidene), 7.29 (2H, d, ^{3}J=8.2Hz, pyridine-*m*-C*H*), 7.37 (2H, t, ^{3}J=1.4Hz, 5-imidazol-2-ylidene), 8.18 (1H, t, ^{3}J=8.2Hz, pyridine *p*-C*H*), 8.41 (2H, br s, imidazol-2-ylidene) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 119.43 (Ar*C*H), 121.21 (Ar*C*H), 128.05 (Ar*C*H), 135.64 (Ar*C*H), 140.95 (Ar*C*H), 168.87 (Ar*C*$_Q$), **MS (EI)** *m/z* (%): 211 (95, M^+) **FTIR (ν_{max} cm^{-1})** KBr 3086 (s), 1725 (s), 1704 (w), 1604 (s), 1581 (s), 1371 (s), 984 (s), 791 (s), 721 (s)

2,6-(di-phenylformamidine)-pyridine 119[467]

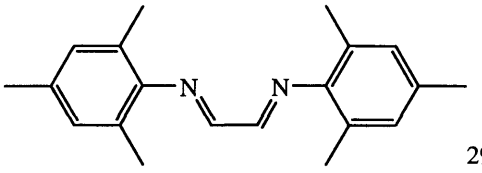


$C_{19}H_{17}N_5$
315.14840 g/mol

The *title compound* was synthesised by addition of *N*-phenylformamide (1.00 g, 8.3 mmol, 2.0 eq) to a solution of 2,6-diaminopyridine (0.45 g, 4.2 mmol, 1.0 eq) and *p*-toluenesulphonic acid (72 mg , 0.4 mmol, 0.1 eq) in ethanol (20 mL, 99.8%) which was heated to reflux for 24 hours. The reaction was cooled to room temperature and the volatiles were removed *in-vacuo*. The residue was dissolved in DCM (20 mL), washed with saturated $NaHCO_3$ (5 mL x 2) and brine (5 mL x 2). The volatiles were removed

in-vacuo and the solid recrystallised from ethanol/ether to give the *title compound* as a white powder (1.20 g, 3.8 mmol, 91%) **Melting point** 198 °C, lit.[467] 196.5 °C **^{1}HNMR** ($CDCl_3$-D_6, 300MHz): δ 7.10 – 7.15 (4H, m, ArC*H*), 7.32 – 7.40 (6H, m, ArC*H*), 7.42 (1H, m, Py-C*H*), 7.51 (2H, m, Py-C*H*), 7.98 (2H, s, =NC*H*N) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 118.14 (Ar*C*H), 118.36 (Ar*C*H), 120.88 (Ar*C*H), 128.25 (Ar*C*H), 137.48 (Ar*C*H), 140.61 (ArC_Q), 145.87 (=N*C*HN), 164.21 (Ar*C*H) **MS (EI)** *m/z* (%): 315 (70, M^+), 196 (45) **FTIR (ν_{max} cm^{-1})** KBr 3391 (br), 3091 (s), 2420 (s), 1612 (w), 1581 (s), 1463 (s), 1391 (s), 1199 (w), 1098 (w), 1005 (s), 864 (s), 839 (s)

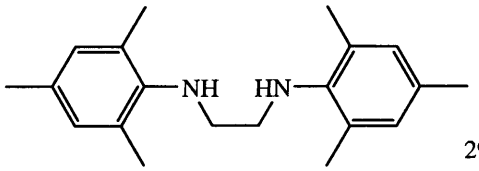
Bis-(2,4,6-trimethy-phenylimino-ethylidene) 121[468]



$C_{20}H_{24}N_2$
292.19395 g/mol

The *title compound* was synthesised by addition of mesityl imidazole (2.0 g, 14.8 mmol, 2.0 eq) to a solution of glyoxal (0.43 g, 7.4 mmol, 1.0 eq) in ethanol (50 mL), which was stirred for 1 hour at room temperature. The yellow precipitate that formed was collected *via* filtration and washed with ethanol to yield a bright yellow solid (1.93 g, 6.44 mmol, 87%) **Melting point** 159 °C, lit.[468] 158 - 159 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.15 (12H, s, *o*-ArCH_3), 2.28 (6H, s, *p*-ArCH_3), 6.90 (4H, s, ArC*H*), 8.09 (2H, s, -N(C*H*)$_2$N- **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 18.75 (*o*-Ar*C*H_3), 20.70 (*p*-Ar*C*H_3), 129.13 (Ar*C*H), 131.26 (*p*-Ar$C_Q$$CH_3$), 132.96 (*o*-Ar$C_Q$$CH_3$), 139.15 (*C*H*C*H), 147.05 (ArC_QN) **MS(EI)** *m/z* (%): 293 (94, M^+H), 146 (100, $C_{10}H_{12}N^-$), 119 (40, $C_9H_{11}^-$) **FTIR (ν_{max} cm^{-1})** KBr 3444 (=NH, br), 3011 (w), 2950 (s), 2914 (s), 2858 (s) 1627 (C=N, s), 1485 (s), 1205 (s), 844 (s)

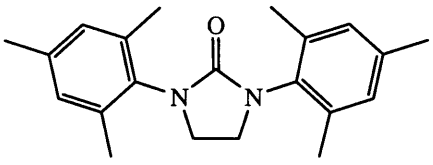
N,N'-Bis-(2,4,6-trimethyl-phenyl)-ethane-1,2,-diamine 122[469]



$C_{20}H_{28}N_2$
296.22525 g/mol

The *title compound* was synthesised by dissolution of bis-(2,4,6-trimethyl-phenylimino-ethylidene) **121** (2.50 g, 8.55 mmol, 1.0 eq) in ethanol (125 mL, 99.6%) and cooling to 0 °C. Sodium borohydride (3.18 g, 85.50 mmol, 10.0 eq) was added portion wise to the reaction solution over 1 hour, maintaining the temperature at 0 °C. The reaction solution was heated to reflux for 1 hour, cooled to room temperature and brine (20 mL) added, which resulted in a white precipitate being formed. The suspension was filtered and the solid washed with water (50 mL x 2). The filtrate and washings were combined and extracted with $CHCl_3$ (60 mL x 2). The organic layer was separated, dried over Na_2SO_4, filtered and the volatiles removed *in-vacuo* to yield a yellow oil, which on standing, crystallised (2.53 g, 8.55 mmol, 100%). **Melting point** 37 – 38 °C, lit.[469] 34 – 36 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.23 (6H, s, *p*-ArC$\underline{H}_3$), 2.28 (12H, s, *o*-ArC$\underline{H}_3$), 3.15 (4H, s, -C$\underline{H}_2$-C$\underline{H}_2$-), 3,24 (2H, br s, N$\underline{H}$), 6.88 (4H, m, ArCH) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 18.41 (*o*-Ar$\underline{C}H_3$), 31.53 (*p*-Ar$\underline{C}$H), 49.15 (-N$\underline{C}H_2$-), 129.46 (Ar$\underline{C}$H), 129.74 (*o*-Ar$\underline{C}_Q$), 131.45 (*p*-Ar$\underline{C}_Q$), 143.34 (Ar$\underline{C}_Q$N) **MS (EI)** *m/z* (%): 297 (65) M^+H, 119 (40) $(C_9H_{11})^-$ **FTIR (ν_{max} cm^{-1})** nujol 3400 (br, NH), 2904 (s), 2790 (s), 2100 (br), 1639 (s), 1273 (s)

1,3-Bis-(2,4,6-trimethyl-phenyl)-imidazolidin-2-one 123[470]

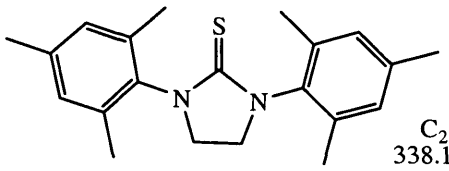


$C_{21}H_{26}N_2O$
322.20451 g/mol

The *title compound* was synthesised by dissolution of *N,N'*-Bis-(2,4,6-trimethyl-phenyl)-ethane-1,2,-diamine **122** (1.86 g, 8.76 mmol, 1.0 eq) in DCM (15 mL) followed by addition of TEA (2.67 mL, 19.27 mmol, 2.2 eq). The solution was cooled to 0 °C

and a solution of triphosgene (2.00 g, 6.75 mmol, 0.35 eq) in DCM (5 mL) was added over 2 hours using a syringe pump, maintaining the temperature of the solution at 0 °C. The reaction was allowed warm to room temperature, and stirred for 2 hours. Filtration of the suspension removed TEA.HCl, and the filtrate was concentrated *in-vacuo*. The crude material was then redissolved in ethyl acetate (15 mL) and washed with saturated sodium bicarbonate solution (5 mL x 3). The organic phase was dried over Na_2SO_4, filtered and the volatiles removed *in-vacuo* to give the *title compound* as a white solid (2.26 g, 7.01 mmol, 78%) **Melting Point** 178 – 181 °C, lit.[470] 175 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.21 (6H, s, *p*-ArC$\underline{H}_3$), 2.30 (12H, s, *o*-ArC$\underline{H}_3$), 3.88 (4H, s -C$\underline{H}_2$-C$\underline{H}_2$-), 6.93 (4H, s, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ18.16 (*p*-Ar$\underline{C}H_3$), 21.00 (*o*-Ar$\underline{C}H_3$), 49.18 (-$\underline{C}H_2$-$\underline{C}H_2$-),129.88 (Ar$\underline{C}$H), 135.24 (*o*-Ar$\underline{C}_Q$CH$_3$), 137.47 (*p*-Ar$\underline{C}_Q$CH$_3$), 138.89(Ar$\underline{C}_Q$N-), 150.49 ($\underline{C}_Q$O) **HRMS (EI)** *m/z* (%): ($C_{21}H_{26}N_2O$) Requires 333.20451, Found: 322.20401 (40, M^+), 119 (70, $C_9H_{11}^+$) **FTIR (ν_{max} cm^{-1})** nujol 3026 (br), 2982 (br), 2933 (s), 1692 (s, C=O), 1510

1,3-Bis-(2,4,6-trimethylphenyl)imidazole-2-thione 124[471]

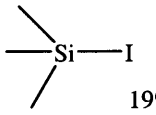


$C_{21}H_{26}N_2S$
338.18167 g/mol

The *title compound* was synthesised by dissolution of *N,N'*-Bis-(2,4,6-trimethyl-phenyl)-ethane-1,2,-diamine **122** (2.20 g, 10.4 mmol, 1.0 eq) in DCM (50 mL), followed by addition of TEA (2.90 mL, 20.8 mmol, 2.0 eq). Thiophosgene (0.8 mL, 10.4 mmol, 1.0 eq) was diluted in DCM (30 mL) and added *via* syringe pump over 2 hours. The dark solution was stirred at room temperature for a further 3 hours. Removal of the volatiles *in-vacuo* and recrystallisation of the dark solid from methanol gave the *title compound* as a white powder (2.67 g, 7.9 mmol, 76%). **Melting Point** 220 °C, lit.[471] 218 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.29 (3H, s, *o*-ArC$\underline{H}_3$,) 2.30 (6H, s, *p*-ArC$\underline{H}_3$), 3.84 (4H, s, -C$\underline{H}_2$-C$\underline{H}_2$-), 6.85 (4H, s, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 18.13 (*o*-Ar$\underline{C}H_3$), 20.97 (*p*-Ar$\underline{C}H_3$), 49.20 (-$\underline{C}H_2$-$\underline{C}H_2$-), 129.86 (Ar$\underline{C}$H), 135.27 (*o*-Ar$\underline{C}_Q$CH$_3$), 137.49 (*p*-Ar$\underline{C}_Q$CH$_3$), 138.89 (Ar$\underline{C}_Q$N-), 150.48 (Ar$\underline{C}_Q$S). **MS FAB** *m/z*

(%): 339 (100, M^+) **FTIR (ν_{max} cm^{-1})** nujol 1488 (s), 1331 (s), 1271 (s), 1205 (s, C=S), 844 (s)

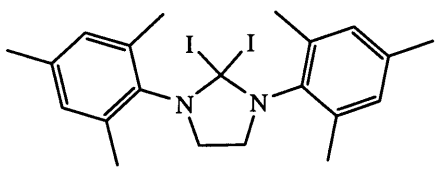
Trimethylsilyl Iodide 129[472]



C_3H_9ISi
199.95182 g/mol

The *title compound* was prepared by a literature method.[472] Aluminium powder (2.80 g, 0.11 mol, 2.1 eq) and hexamethyldisiloxane (10.6 mL, 50.00 mmol, 1.0 eq) were added to a 100 mL 3 necked flask fitted with a condenser, and purged with nitrogen, then warmed to 60 °C. Iodine (25.40 g, 0.10 mol, 2.0eq) was added portion wise over 1 hour. The solution turned purple on each addition of I_2, returning to a grey colour after its consumption. Once addition of I_2 was completed, the reaction was heated to reflux (160 °C) for 2 hours. The reaction was cooled to room temperature and the apparatus rearranged for the distillation of the suspension with a Bunsen burner. The *title compound* distilled at 109 °C as a colourless liquid (15.1 g, 38.00 mmol, 76%) **^{1}HNMR** ($CDCl_3$, 500MHz): δ 0.76 (9H, s, $(C\underline{H}_3)_3SiI$ **^{13}CNMR** ($CDCl_3$, 125.7MHz): δ 5.70 $(\underline{C}H_3)_3SiI$ **MS (CI)**: ammonia, *m/z* (%) 127 (70, I^+), 80 (55) **FTIR (ν_{max} cm^{-1})** neat 1022 (s, Si-I), 907 (s, SiCH3), 800 (s), 725 (s)

2,2-Diiodo-1,3-bis-(2,4,6-trimethylphenyl)imidazolidine 130

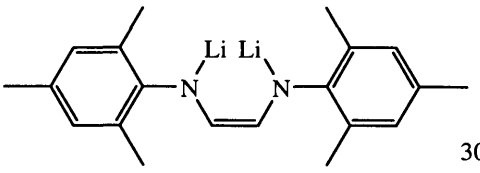


$C_{21}H_{26}I_2N_2$
560.01854 g/mol

The *title compound* was synthesised by addition of 1,3-Bis-(2,4,6-trimethyl-phenyl)-imidazolidin-2-one C$XX (250 mg, 1.1 mmol, 1.0 eq) to a stirred mixture of TMSI

C$XX (2.5 mL, 17.5 mmol, 16.7 eq) and TMSOTf (0.5 mL, 2.92 mmol, 2.78 eq) and heated to reflux (115 °C) for 12 hours under a N_2 atmosphere. A red oil, immiscible with the reaction solution formed during this time and was transferred *via* cannula to a second flask under N_2 once the reaction had cooled to room temperature. Removal of the volatiles *in-vacuo* from this oil resulted in material whose data were consistent with the expected product. Instability of the *title compound* precluded complete characterisation (82 mg, 0.15mM, 14%) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.16 (6H, s, *p*-ArC$\underline{H}_3$), 2.31 (12H, s, *o*-ArC$\underline{H}_3$), 3.86 (4H, s -C$\underline{H}_2$-C$\underline{H}_2$-), 6.94 (4H, m, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 18.73 (*p*-Ar$\underline{C}H_3$), 21.11 (*o*-Ar$\underline{C}H_3$), 48.08 (-$\underline{C}H_2$-$\underline{C}H_2$-), 109.57 ($\underline{C}_QI_2$) 129.99 (Ar$\underline{C}$H), 136.37 (*o*-Ar$\underline{C}_QCH_3$), 139.28 (*p*-Ar$\underline{C}_QCH_3$), 139.55 (Ar$\underline{C}_Q$N-) **MS ES** *m/z* (%): 560 (5, M^+), 433 (10, M^+-I), 293 (65)

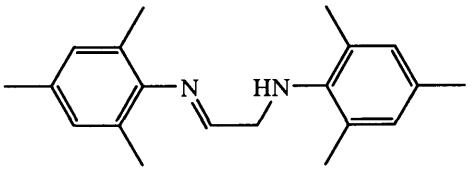
_N,N_-Bis(2,4,6-trimethylphenyl)-ethene-1,2-diaminio bis-lithio salt 131[473]



$C_{20}H_{24}Li_2N_2$
306.22595 g/mol

The *title compound* was synthesised by cooling a solution of Bis-(2,4,6-trimethyphenylimino-ethylidene) **130** (4.00 g, 19.21 mmol, 1.0 eq) to –78 °C in THF (40 mL). Li^0 (293 mg, 42.26 mmol, 2.2 eq), was added and if the reaction did not initiate (red colouration around the metal surface), the flask was exposed to sonication for 10-15 seconds. The reaction was stirred for 12 hours at room temperature, to give a red solution. The attempted transfer *via* stainless steel cannula resulted in a rapid colour change of the transferred solution to black. The crude solution was therefore used, without any formal workup, thus precluding full structural characterisation. **^{1}HNMR** (THF-D_8, 300MHz): δ 2.16 (12H, s, *o*-ArC$\underline{H}_3$), 2.28 (6H, s, *p*-ArC$\underline{H}_3$), 6.89 (4H, s, ArC$\underline{H}$), 8.12 (2H, s, NC$\underline{H}$=C$\underline{H}$N) **^{13}CNMR** (THF-D_8, 75.5MHz): δ 17.89 (*p*-Ar$\underline{C}H_3$), 20.43 (*o*-Ar$\underline{C}H_3$), 126.22 (*o*-Ar$\underline{C}_QCH_3$), 128.62 (Ar$\underline{C}$H), 133.87 (*p*-Ar$\underline{C}_QCH_3$), 147.11(Ar$\underline{C}_Q$N), 163.25 (N$\underline{C}$H=$\underline{C}$HN) Red solution in THF, not isolated

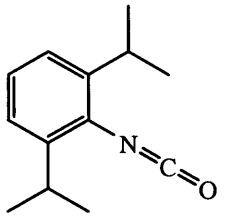
_N_-(2-mesitylamino)ethylidene)-mesitylamine 133[473]



$C_{20}H_{26}N_2$
294.2096 g/mol

A sample of *N,N*-Bis(2,4,6-trimethylphenyl)-ethene-1,2-diaminio bis-lithio salt **131** in THF (1 mL) when quenched with saturated NH_4Cl (0.5 mL) yields the *title compound.* The aqueous solution was extracted with DCM (2 mL) and dried *in-vacuo* to provide a colourless oil as an analytical sample.[473] **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.96 (6H, s, *o*-ArC$\underline{H}_3$), 2.00 (6H, s, *o*-ArC$\underline{H}_3$), 2.04 (3H, s, *p*-ArC$\underline{H}_3$), 2.12 (3H, s, *p*-ArC$\underline{H}_3$), 3.95 (2H, br s. ArNHC$\underline{H}_2$-), 6.56 (2H, s, ArC$\underline{H}$), 6.72 (2H, s, ArC$\underline{H}$), 7.94 (1H, d, ^{3}J=2.3Hz, ArN=C$\underline{H}$-CH_2-) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 17.08 (*p*-Ar$\underline{C}H_3$), 17.80 (*p*-Ar$\underline{C}H_3$), 19.99 (*o*-Ar$\underline{C}H_3$), 20.35 (*o*-Ar$\underline{C}H_3$), 67.45 (ArNH$\underline{C}H_2$-) 121.29 (*o*-Ar$\underline{C}_Q$$CH_3$), 126.07 (*o*-Ar$\underline{C}_Q$$CH_3$) 126.36 (Ar$\underline{C}_Q$), 128.44 (Ar$\underline{C}$H) 128.64 (Ar$\underline{C}$H), 133.76 (Ar$\underline{C}_Q$), 139.87 (Ar$\underline{C}_Q$), 147.12 (Ar$\underline{C}_Q$), 163.06 (Ar-N=$\underline{C}$H) **MS EI** *m/z* (%): 294 (90, M^+) **FTIR (ν_{max} cm^{-1})** KBr 3350 (s, NH), 1658 (s, C=N), 1568 (br), 1436 (s), 821 (s)

2,6 Diisopropylphenyl isocyanate 134[474]

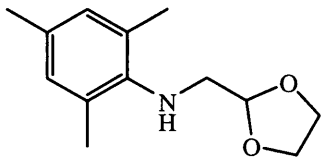


$C_{13}H_{17}NO$
203.13101 g/mol

The *title compound* was synthesised by addition of phosgene (17.7 mL of a 20% toluene solution, 3.4 mM, 1.2 eq) to a vigorously stirred solution of 2,6 di-*iso*propylaniline (0.5 g, 2.8 mmol, 1.0 eq) and TEA (0.86 mL, 6.2 mmol, 2.2 eq) in toluene (10 mL). The solution was refluxed for 4 hours, cooled to room temperature, and the volatiles removed *in-vacuo*. The resulting solid was extracted with diethyl ether (10 mL x 3) and the combined organic phases were concentrated *in-vacuo* to give a clear oil (0.5 g, 2.5 mmol, 89%) with analytical data concordant with that in the lit.[474] **^{1}HNMR** (C_6D_6, 300MHz): δ 0.79 (6H, s, -CH(C$\underline{H}_3$)$_2$), 0.82 (6H, s, -CH(C$\underline{H}_3$)$_2$), 2.83 (2H, sep,

^{3}J=6.8Hz, -C$\underline{H}$(CH$_3$)$_2$), 6.66 (3H, m, ArC$\underline{H}$) **^{13}CNMR** (C$_6$D$_6$, 75.5MHz): δ 22.83 (-CH($\underline{C}$H$_3$)$_2$), 29.80 (-$\underline{C}$H(CH$_3$)$_2$), 123.63 (*m*-Ar$\underline{C}$H), 126.38 (*o*-Ar$\underline{C}$H), 129.20 (Ar$\underline{C}_Q$N), 129.28 (Ar$\underline{C}_Q$CH(CH$_3$)$_2$), 143.20 (-N$\underline{C}_Q$O) **MS EI** *m/z* (%) 203 (45, M$^+$), 170 (30, M-(C$_3$H$_7$)$^-$) **FTIR (ν_{max} cm^{-1})** neat 3068 (s), 2965 (s), 2931 (br), 2868 (s), 2292 (s, N=C=O), 2263 (s, N=C=O), 1604 (s), 1598 (s), 1468 (s), 1173 (s), 1046 (s), 1002 (s), 796 (s)

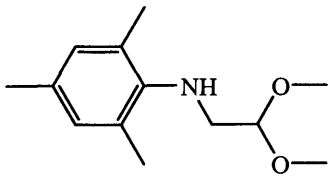
[1,3]-Dioxolan-2-ylmethyl-(2,4,6-trimethylphenyl)amine 135



C$_{13}$H$_{19}$NO$_2$
221.14158 g/mol

The *title compound* was synthesised by stirring mesityl amine (1.03 mL, 7.4 mmol, 1.0 eq) and Cs$_2$CO$_3$ (2.65 g, 8.1 mmol, 1.1 eq) at room temperature in DCM (20 mL) for 30 minutes. 2-(bromomethyl)-1,3-dioxolane (0.77 mL, 7.4 mmol, 1.0 eq) was added and the reaction stirred for a further 12 hours at room temperature. The suspension was filtered, washed with saturated sodium bicarbonate solution (5 mL), water (5 mL) and brine (5 mL). Removal of the volatiles *in-vacuo* gave a yellow oil (1.63 g, 7.4 mmol, 100%) **^{1}HNMR** (CDCl$_3$, 300MHz): δ 2.14 (6H, s, *o*-ArC$\underline{H}_3$) 2.19 (3H, s, *p*-ArC$\underline{H}_3$), 3.37 (2H, d, ^{3}J=4.0Hz, -NC$\underline{H}_2$CH-), 3.92 (2H, m, OC$\underline{H}_2$CH$_2$O), 4.04 (2H, m, OCH$_2$C$\underline{H}_2$O), 5.13 (1H, dt, ^{3}J=4.0, 4.1Hz, $\underline{H}$C(OCH$_2$CH$_2$O)), 6.75 (2H, m, ArC$\underline{H}$) **^{13}CNMR** (CDCl$_3$, 75.5MHz): δ 17.35 (*p*-Ar$\underline{C}$H$_3$), 20.18 (*o*-Ar$\underline{C}$H$_3$), 32.34 (-N$\underline{C}$H$_2$CH-), 65.51 (-O$\underline{C}$H$_2\underline{C}$H$_2$O-), 101.90 (-H$\underline{C}$(OCH$_2$CH$_2$O)), 121.60 (*o*-Ar$\underline{C}_Q$CH$_3$), 126.82 (Ar$\underline{C}_Q$N), 128.65 (Ar$\underline{C}$H), 140.02 (*p*-Ar$\underline{C}_Q$CH$_3$) **HRMS (EI)** *M/z* (%): C$_{13}$H$_{19}$NO$_2$ Requires 221.14103, Found: 221.14120221 (65, M$^+$), 148 (95, M-(C$_3$H$_5$O$_2$)$^-$), 135 (95, Mesityl aniline) **FTIR (ν_{max} cm^{-1})** neat 3396 (s, NH), 2978 (br), 2904 (br), 2856 (s), 2365(s), 2335(s), 2256(s), 1596 (s), 1564 (s), 1432 (s), 876 (s)

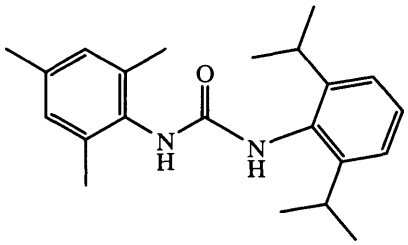
(2,2-Dimethoxyethyl)-(2,4,6-trimethylphenyl)amine 136



$C_{13}H_{21}NO_2$
223.15723 g/mol

The *title compound* was synthesised by stirring mesityl amine (1.03 mL, 7.4 mmol, 1.0 eq) and Cs_2CO_3 (2.65 g, 8.1 mmol, 1.1 eq) at room temperature in DCM (20 mL) for 30 minutes. 2-chloro-1,1-dimethoxyethane (1.01 mL, 7.4 mmol, 1.0 eq) was added, and the reaction stirred for a further 12 hours at room temperature. The suspension was filtered, washed with saturated sodium bicarbonate solution (5 mL), water (5 mL) and brine (5 mL). Removal of the volatiles *in-vacuo* gave a pale brown oil (1.67 g, 7.4 mmol, 100%) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.17 (6H, s, *o*-ArC$\underline{H}_3$,) 2.23 (3H, s, *p*-ArC$\underline{H}_3$), 3.43 (6H, s, 2 -OC$\underline{H}_3$), 3.52 (2H, d, ^{3}J=5.8Hz, (-NC$\underline{H}_2$CH-), 4.53 (1H, dd, ^{3}J=5.5Hz, -NCH$_2$C$\underline{H}$-), 6.78 (2H, m, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 17.55 (*p*-Ar$\underline{C}$H$_3$), 20.50 (*o*-Ar$\underline{C}$H$_3$), 38.26 (-N$\underline{C}$H$_2$CH-), 58.40 (-O$\underline{C}$H$_3$), 101.58 (-H$\underline{C}$(OCH$_3$)$_2$), 121.92 (*o*-Ar$\underline{C}_Q$CH$_3$), 127.20 (Ar$\underline{C}_Q$N), 129.37 (Ar$\underline{C}$H), 138.40 (*p*-Ar$\underline{C}_Q$CH$_3$) **HRMS (EI)**: *M/z* (%) ($C_{13}H_{21}NO_2$) Requires 223.15668, Found: 223.15679 (80) M^+, 207 (100) –CH_3, 135 (100) Mesityl aniline, 120 (100) Mesitylene **FTIR (ν_{max} cm^{-1})** neat 3396 (br, NH), 3002 (s), 2974 (br) 2954 (s), 2918 (s), 2860 (s, OMe), 2354 (w), 2335 (s), 2251 (w), 1531 (s), 1445 (s), 851 (s)

1-(2,6-Diisopropyl-phenyl)-3-(2,4,6-trimethyl-phenyl)-urea 137

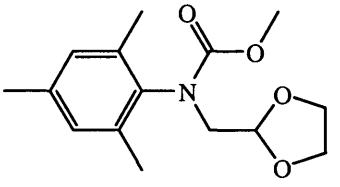


$C_{22}H_{30}N_2O$
338.23581 g/mol

The *title compound* was synthesised by addition of DMAP (90.4 mg, 0.74 mmol, 0.1 eq) to a stirred solution of $(BOC)_2O$ (1.69 g, 7.8 mmol, 1.05 eq) in DCM (10 mL). Mesityl aniline (1.04 mL, 7.4 mmol, 1.0 eq) was added dropwise to the reaction solution, which was stirred at room temperature for 30 minutes. A single addition of 2,6-di-

*iso*propylphenyl aniline (1.46 mL, 7.8 mmol, 1.05 eq) was made and the solution heated to reflux for 40 hours. The white suspension was cooled to room temperature and the volatiles removed *in-vacuo* to give a white solid that was recrystallised from acetone to provide the *title compound* as white needles (1.37 g, 4.0 mmol, 86%). **Melting point** 213 – 215 °C **^{1}HNMR** ($CDCl_3$, 400MHz, 328K): δ 1.22 (12H, br s, $(C\underline{H}_3)_2CH$), 2.25 (3H, s, *p*-Ar$C\underline{H}_3$), 2.29 (6H, br s, *o*-Ar$C\underline{H}_3$), 3.17(1H, br s, $(CH_3)_2C\underline{H}$), 3.54 (1H, br s, $(CH_3)_2C\underline{H}$), 5.48 (1H, br s, N$\underline{H}$), 6.89 (2H, br s., Mesityl Ar$C\underline{H}$), 7.17 (2H, br d, ^{3}J=7.4Hz, Diisopropyl *m*-Ar$C\underline{H}$), 7.26 (1H, t, ^{3}J=7.4Hz, Diisopropyl *p*-Ar$C\underline{H}$) **^{13}CNMR** ($CDCl_3$, 100.75MHz, 328K): δ 18.21 (*o*-Ar$\underline{C}H_3$), 20.88 (*p*-Ar$\underline{C}H_3$), 22.52 ($(\underline{C}H_3)_2CH$) 23.65 (br, $(\underline{C}H_3)_2CH$), 28.63 ($(\underline{C}H_3)_2CH$), 118.70 (Diisopropyl *p*-Ar$\underline{C}H$), 123.72 (br, Diisopropyl *m*-Ar$\underline{C}H$), 129.38 (br, Mesityl Ar$\underline{C}H$), 131.57 (*p*-Ar$\underline{C}_Q CH_3$), 131.74(Diisopropyl-Ar$\underline{C}_Q N$), 136.48 (br, *o*-Ar$\underline{C}_Q CH_3$), 140.35 (Mesityl-Ar$\underline{C}_Q N$), 144.02 (Ar$\underline{C}_Q CH(CH_3)_2$), 155.90 ($\underline{C}_Q O$) **HRMS (EI)** *M/z* (%): ($C_{22}H_{30}N_2O$) requires 338.23581, Found : 338.23633 (20, M^+), 162 (20), 135 (100) **FTIR (ν_{max} cm^{-1})** KBr 3296 (br), 2960 (s), 2925 (s), 2879 (s), 1637 (s), 1551 (s), 1479 (br), 1245 (s) 803 (s), 731 (s)

1,3-dioxolane-2,4,6-trimethylphenyl-carbamic acid methyl ester 138[475]

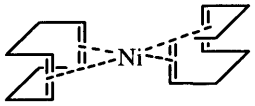


$C_{15}H_{21}NO_4$
279.14706 g/mol

The *title compound* was synthesised by addition of TEA (1.7 mL, 12.4 mmol, 1.1 eq) and DMAP (130 mg, 1.1 mmol, 0.1 eq) to a solution of mesityl dioxolane **135** (2.5 g, 11.3 mmol, 1.0 eq) in ether (100 mL). Methyl chloroformate (0.87 mL, 11.3 mmol, 1.0 eq) was added to the yellow solution, and the reaction stirred for 2 hours before it was filtered. The solids were extracted into ether (1 x 20 mL), which was washed with water (20 mL) and brine (20 mL). Filtration through a short plug of silica followed by removal of the volatiles *in-vacuo* gave the *title compound* as a cream coloured solid (2.1 g, 7. 6 mmol, 67%) **Melting point** 220 °C (decomp.), lit.[475] 222 °C (decomp.) **^{1}HNMR** (DMSO-D_6, 300MHz): δ 2.20 (6H, s, *o*-Ar$C\underline{H}_3$), 2.25 (3H, s, *p*-Ar$C\underline{H}_3$), 3.65 (2H, dd, ^{3}J=3.8Hz, -N$C\underline{H}_2$CH-), 3.77 (3H, s, -O$C\underline{H}_3$), 4.01 (2H, m, -O$C\underline{H}_2CH_2$O-), 4.11 (2H, m,

-OC$\underline{H}_2$CH$_2$O-), 5.23 (1H, dt, 3J=3.9, 4.0Hz, -CH$_2$C$\underline{H}$-), 6.77 (2H, m, ArC$\underline{H}$) **^{13}CNMR** ((DMSO-D$_6$, 75.5MHz): δ 18.65 (*p*-Ar$\underline{C}$H$_3$), 20.41 (*o*-Ar$\underline{C}$H$_3$), 51.48 (-N$\underline{C}$H$_2$CH-), 53.92 (-OC$\underline{H}_3$) 65.88 (-O$\underline{C}$H$_2\underline{C}$H$_2$O-), 107.45 (-H$\underline{C}$(OCH$_2$CH$_2$O)), 126.88 (Ar$\underline{C}$H), 132.00 (*o*-Ar$\underline{C}_Q$CH$_3$), 137.18 (Ar$\underline{C}_Q$N), 137.22 (*p*-Ar$\underline{C}_Q$CH$_3$), 159.70 (-N$\underline{C}_Q$OCH$_3$) **MS EI** *m/z* (%): 279 (85, M$^+$), 220 (25, M$^+$-C$_2$H$_3$O$_2$) **FTIR (ν_{max} cm^{-1})** KBr 2978 (s), 2906 (s), 2821 (s), 1709 (w), 1611 (s), 1488 (s), 1406 (s), 1312 (w), 1257 (s), 992 (s), 776 (s)

Bis(1,5-cyclooctadiene)nickel (0) 145[476]



C$_{20}$H$_{36}$Ni
334.21705 g/mol

The *title compound* was prepared according to a literature method.[476] Technical grade bis(acetylacetonate)nickel(II) (4.67 g, 18.2 mmol, 1.0 eq) was added to a two necked vessel that was fitted with a dropping funnel, and heated *in-vacuo* using a heat gun, until it developed a homogeneous light blue colour. The solid was cooled to room temperature and a positive nitrogen atmosphere established, before it was suspended in tetrahydrofuran (25 mL). Freshly distilled 1,5-cyclooctadiene (7.9 3g, 72.3 mmol, 4.0 eq) was added, and the suspension was cooled to -78 °C, giving a green slurry. A 1.0 M solution of DIBAH (45.4 mL, 45.4 mmol, 2.5 eq) in THF was transferred to the dropping funnel and added to the reaction over 1 hour, to give a dark, reddish brown solution, which over 1 hour was allowed to warm to 0 °C. The solution was treated with diethyl ether (65 mL) to give a light yellow precipitate, then cooled to -78 °C for 12 hours without stirring, to complete the precipitation. The product was isolated by filtration at -78 °C *via* a filter paper tipped cannula, washed with cold diethyl ether (15 mL portions) until all the brown residues were removed, and dried *in-vacuo*. The pale yellow solid was dissolved in minimal toluene at room temperature and rapidly filtered through celite, under N_2, to remove metallic nickel. After 12 hours at -78 °C, the deep yellow supernatant was removed at -78 °C through a filter paper tipped cannula, to give bright yellow needles, which after pentane washes (2 x 15 mL), gave the *title compound* (0.86 g, 2.7 mmol, 14% based on Ni(acac)$_2$). The physical and spectral properties of this compound were identical to those stated in the original paper.[476]

Transfer hydrogenation - General methods

Below are listed some of the key methods which were investigated when trying to determine suitable conditions for the reduction of substrates using our ruthenium based complexes. Chapter 4 of this thesis discusses their development and demonstrates their effectiveness with a broad range of substrates.

Transfer hydrogenation method A (Ethylene glycol)

Ruthenium complex (5 mol%) was added to a refluxing solution of substrate (1.0 mmol) in ethylene glycol (3 mL). The solution was refluxed overnight, cooled to room temperature and extracted with benzene (20 mL x 2). The combined benzene solutions were washed with water (10 mL), dried, filtered and the volatiles removed *in-vacuo*.

Transfer hydrogenation method B (propan-2-ol)

NaOH (40.0 mg, 10 mol%), and ruthenium complex (0.03 mol%) were added to a solution of aldehyde (10.0 mmol) in propan-2-ol (5 mL, 2.0 M). The solution was refluxed for 24 hours, cooled to room temperature and the volatiles removed *in-vacuo*. The viscous yellow oil was extracted with ether and purified by column chromatography to yield the corresponding alcohol.

Transfer hydrogenation method C (propan-2-ol)

KO^{t}Bu (112.0 mg, 10 mol%), and ruthenium complex (0.015 mol%) were added to propan-2-ol (5 mL, 2.0 M) and heated to reflux for 45 minutes. Aldehyde (10.0 mmol) was added and the solution was refluxed for 24 hours, before being cooled to room temperature to provide a red solution containing viscous red oil. The reaction was quenched by the addition of HCl (2 mL, 2M) and the volatiles were removed *in-vacuo* to give a yellow viscous oil. Extraction of the oil into petroleum spirit and purification by chromatography gave the corresponding product. An alternative method to quench the reaction required the reaction be cooled to room temperature and petroleum spirit (10 mL) added. The red solution was washed with water (5 mL), and the volatiles removed *in-vacuo* to give a red viscous oil, which was purified by column chromatography. The yields obtained by the two quench methods were comparable.

Transfer hydrogenation method D (propan-2-ol)

KO^{t}Bu (112.0 mg, 10 mol%) and ruthenium complex (0.015 mol%) were added to propan-2-ol (5 mL) and stirred at room temperature for 45 minutes. Aldehyde (10.0 mmol) was added and the solution was stirred for 3 weeks, to provide a red solution containing a viscous red oil. An addition of petroleum spirit (10 mL) was made to the reaction and the red solution was washed with water (5 mL). The volatiles were removed *in-vacuo* to give a red viscous oil, which was purified by column chromatography.

General method for transfer hydrogenation of aldehydes using propan-2-ol

Ruthenium complex (0.03 mol%) was added to refluxing propan-2-ol (5 mL) for a 45-minute incubation period, after which aldehyde (10.0 mmol) and K_2CO_3 (0.5 eq) were added, and the reaction maintained at reflux for 12 hours. The reaction was cooled to room temperature, filtered and the volatiles removed *in-vacuo*. The residue was extracted into petroleum spirits (or ether) and purified *via* column chromatography.

General method for transfer hydrogenation of ketones using propan-2-ol

Ruthenium complex (0.03 mol%)was added to refluxing propan-2-ol (5 mL) for a 45-minute incubation period, after which substrate (1.0 eq) and K_2CO_3 (2.0 eq) were added, and the reaction maintained at reflux for 12 hours. The reaction was cooled to room temperature, filtered and the volatiles removed *in-vacuo*. The residue was extracted into petroleum spirits (or ether) and purified *via* column chromatography

Transfer hydrogenation method E (formic acid)

Ruthenium complex (0.03 mol%) was added to formic acid (5 mL) for a 45-minute incubation period at reflux, after which aldehyde (10.0 mmol) was added, and the reaction maintained at reflux for 12 hours. The reaction was cooled to room temperature, diluted with water (10 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic fractions were washed with brine, dried, filtered and the volatiles removed *in-vacuo*. The residue was purified *via* column chromatography.

Transfer hydrogenation method E (formic acid)

Ruthenium complex (0.03 mol%) was added to formic acid/TEA azeotrope (5 mL) for a 45-minute incubation period at 90 °C, after which aldehyde (10.0 mmol) was added, and the reaction maintained at 90 °C for 12 hours. The reaction was cooled to room temperature, diluted with water (10 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic fractions were washed with brine, dried, filtered and the volatiles removed *in-vacuo*. The residue was diluted in methanol and refluxed for 1 hour, before being cooled to room temperature and the volatiles removed *in-vacuo*. The residue was purified *via* column chromatography.

General method for transfer hydrogenation of aldehydes using formic acid

Ruthenium complex (0.03 mol%) was added to formic acid/TEA azeotrope (5 mL, 5/2 mol/mol) for a 45-minute incubation period at reflux, after which aldehyde (10.0 mmol) was added, and the reaction maintained at reflux for 12 hours. The reaction was cooled to room temperature, diluted with water (10 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic fractions were washed with brine, dried, filtered and the volatiles removed *in-vacuo*. The residue was purified *via* column chromatography.

General method for transfer hydrogenation of aldehydes using formic acid/Ionic liquid

Ruthenium complex (0.03 mol%) and formic acid/TEA azeotrope (10.0 eq) was added to the ionic liquid (5 mL) for a 45-minute incubation period at 150 °C, after which aldehyde (10.0 mmol) was added, and the reaction maintained at 150 °C for 40 hours. The reaction was cooled to room temperature, and extracted with ethyl acetate (10 mL x 3). The combined organic fractions were washed with water (10 mL) and brine, dried, filtered and the volatiles removed *in-vacuo*. The residue was purified *via* column chromatography.

Transfer hydrogenation products

All of the following compounds were analysed by ^{1}HNMR, ^{13}CNMR and where appropriate, melting point and were found to have identical spectral and physical properties to authentic samples.

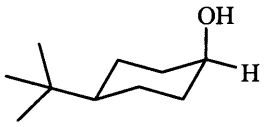
Aldehydes

4-Methylbenzyl alcohol	4-Bromobenzyl alcohol	4-Methoxybenzyl alcohol
Benzyl alcohol	3-Phenyl-prop-2-en-1-ol	4-Nitrobenzyl alcohol
3-Methylbenzyl alcohol	3-Bromobenzyl alcohol	3-Methoxybezyl alcohol
3-Nitrobenzyl alcohol	2-Methylbenzyl alcohol	2-Bromobenzyl alcohol
2-Methoxybenzyl alcohol	2-Nitrobenzyl alcohol	4-Dimethylaminobenzyl alcohol
3-Hydroxy-4-methoxybenzyl alcohol	2-Hydroxy-5-methoxybenzyl alcohol	2-Methoxy-5-bromobenzyl alcohol
2,4,6-trimethylbenzyl alcohol	4-Hydroxybenzaldehyde	Furfuryl alcohol
3-Phenyl-propanol	3-Cylohexylpropan-1-ol	Cyclohexylmethanol
3,7-dimethyloct-6-en-1-ol		

Ketones

1-Phenyl-ethanol	1-Phenyl-propan-1-ol	2-Methyl-1-phenyl-propan-1-ol
cis-4-*tert*-butylCyclohexanol	*trans*-4-*tert*-butylCyclohexanol	*cis*-3,3,5-trimethylcyclohexanol
trans-3,3,5-trimethylcyclohexanol	1-phenyl-1-butanol	2-Methyl-1-phenylpropanol
1-(2-Chlorophenyl)ethanol	Trifluoromethyl Benzyl alcohol	Cyclopentanol
Cyclohexanol	6-methylhept-5-en-2-ol	Cyclodecanol
Phenol	Dicyclopropyl methanol	*trans*-4-*tert*-butyl cyclohexanol formate ester
cis-4-*tert*-butyl cyclohexanol formate ester		

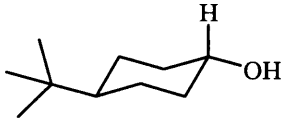
cis-4-_tert_-ButylCyclohexanol 201[477,478]



$C_{10}H_{20}O$
156.15141 g/mol

The *title compound* was prepared by a literature method in order to provide an authentic sample.[477] To a stirred solution of L-selectride (48.7 mL, 48 mmol, 1.5 eq) in THF (50 mL) at -78 °C, a solution of 4-*tert*-butylcyclohexanone (5.01 g, 32 mmol, 1.0 eq) in THF (25 mL) was added dropwise. The temperature was maintained at -78 °C for 2 hours before the reaction mixture was allowed to warm to room temperature and stirred for a further 12 hours. The mixture was cooled to 0 °C, quenched with water (10 mL) and warmed to room temperature. An addition of sodium hydroxide (20 mL, 3 M) was made, followed by hydrogen peroxide (20 mL, 30% aqueous solution) and was then stirred for 2 hours. The mixture was extracted with Et_2O (3 x 50 mL), and the combined organic fractions were washed with water (15 mL) and saturated NaCl solution (15 mL), dried, filtered and the volatiles removed *in vacuo* to yield the *title compound* as a white solid. (4.61 g, 29.52 mmol, 91%) **Melting point** 81 – 83 °C, lit.[478] 82 – 83 °C **^{1}HNMR** ($CDCl_3$, 500MHz): δ 0.87 (9H, s, -C(C$\underline{H}_3$)$_3$), 1.32 – 1.88 (m, 9H), 4.02 (1H br t, ^{3}J=2.3Hz, equatorial C$\underline{H}$OH) **^{13}CNMR** ($CDCl_3$, 125.7MHz): δ 20.86 (-C($\underline{C}$H$_3$)$_3$), 27.40 (-$\underline{C}$H$_2$-), 32.55 (-$\underline{C}_Q$(CH$_3$)$_3$), 33.38 (-$\underline{C}$H$_2$-), 48.01 (-$\underline{C}_Q$C(CH$_3$)$_3$), 65.52 (-$\underline{C}$HOH) **MS EI** *m/z* (%): 123 (25), 99 (20), 81 (50), 57 (100) **FTIR (ν_{max} cm^{-1})** KBr 3281 (OH, br), 2963 (br), 2857 (br), 1477 (br), 1436 (br), 1199 (s), 1042 (s), 1012 (s), 966 (s)

trans-4-_tert_-ButylCyclohexanol 202[477,478]

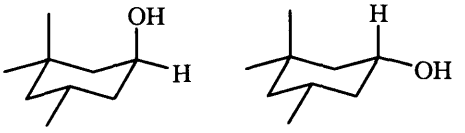


$C_{10}H_{20}O$
156.15141 g/mol

The *title compound* was prepared by a literature method in order to provide an authentic sample.[477] To a suspension of lithium aluminium hydride (1.84 g, 49.0 mmol, 1.5 eq) in Et_2O (40 mL) at 0 °C, a solution of 4-*tert*-butylcyclohexanone (5.13 g, 33.0 mmol) in Et_2O (25 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 2 hours

before quenching with water (10 mL). The suspension was filtered through celite and the filtrate extracted with Et_2O (3 x 50 mL). The combined organic fractions were washed with water, dried, filtered and the volatiles removed *in vacuo* to yield the *title compound* as a white solid (3.11 g, 19.9 mmol, 59%) **Melting point** 77 – 79 °C, lit.[478] 81 – 82 °C **^{1}HNMR** ($CDCl_3$, 500MHz): δ 0.77 (9H, s, -C(C$\underline{H}_3$)$_3$), 0.95 – 2.01 (m, 9H), 3.50 (1H sep, ^{3}J= 4.6, axial -C$\underline{H}$OH) **^{13}CNMR** ($CDCl_3$, 125.7MHz): δ 25.57 (-C($\underline{C}H_3$)$_3$), 27.40 (-$\underline{C}_Q$(CH$_3$)$_3$), 32.22 (-$\underline{C}H_2$-), 35.88 (-$\underline{C}H_2$-), 47.13 (-$\underline{C}_Q$C(CH$_3$)$_3$), 71.02 (-$\underline{C}$HOH) **MS EI** *m/z* (%): 123 (25), 99 (20), 81 (50), 57 (100) **FTIR (ν_{max} cm^{-1})** KBr 3251 (OH, br), 2948 (br), 2862 (s), 1472 (br), 1451 (br), 1364 (s), 1072 (s), 981 (s), 900 (s)

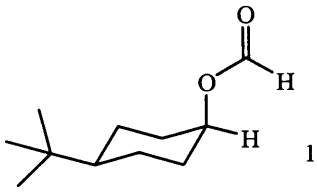
***cis*- and *trans*-3,3,5-trimethylcyclohexanol 203, 204**[479]



$C_9H_{18}O$
142.13577 g/mol

The *title compounds* were isolated as an oil that contained the inseparable pair of stereoisomers in the ratio 1:3.6 axial OH **203**: equatorial OH **204** as determined by ^{1}H NMR. **^{1}HNMR** ($CDCl_3$, 300MHz): δ 0.96 (2H, m, C$\underline{H}_2$), 0.80 – 1.11 (10H, m), 1.26 (1H, m), 1.59 (1H, m), 1.88 (1H, m), 2.73 (1H, br s), 3.69 (1H, m, equatorial C$\underline{H}$OH), 4.07 (1H, m, axial C$\underline{H}$OH) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 22.61 ($\underline{C}H_3$), 22.70 ($\underline{C}H_3$), 25.72 ($\underline{C}H_3$), 22.84 ($\underline{C}H_3$) 27.19 ($\underline{C}$H), 28.17 ($\underline{C}$H), 30.74 ($\underline{C}_Q$), 31.88 ($\underline{C}_Q$), 33.09 ($\underline{C}H_3$), 34.14 ($\underline{C}H_3$), 41.56 ($\underline{C}H_2$), 44.54 ($\underline{C}H_2$), 44.79 ($\underline{C}H_2$), 48.50 ($\underline{C}H_2$), 47.67 ($\underline{C}H_2$), 48.07 ($\underline{C}H_2$), 67.53 ($\underline{C}$HOH), 68.29 ($\underline{C}$HOH) **MS EI** *m/z* (%): 109 (100), 83 (55), 41 (55) **FTIR (ν_{max} cm^{-1})** neat 3346 (br), 2948 (w), 2914 (s), 1460 (s), 1364 (s), 1240 (s), 1183 (s), 1148 (s), 1080 (s), 1026 (s) 760 (s)

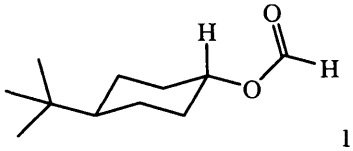
cis-4-_tert_-ButylCyclohexanol formate ester 221[480]



$C_{11}H_{20}O_2$
184.14633 g/mol

Melting Point 34 – 36 °C, lit.[480] melting point not quoted **^{1}HNMR** ($CDCl_3$, 500MHz): δ 0.85 (9H, s, -C(C<u>H</u>$_3$)$_3$), 0.97 – 2.41 (m, 9H), 4.75 (1H sep, ^{3}J=4.6Hz, axial -C<u>H</u>OH), 8.03 (1H, s, OCO<u>H</u>) **^{13}CNMR** ($CDCl_3$, 125.7MHz): δ 27.62 (-C(<u>C</u>H$_3$)$_3$), 70.92 (-<u>C</u>HOH), 160.74 (O<u>C</u>OH) **MS EI** *m/z* (%): 156 (10, M-HCO), 147 (30), 57 (100, $C_4H_9^+$)

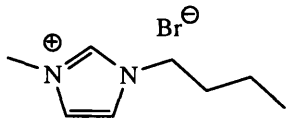
trans-4-_tert_-ButylCyclohexanol formate ester 222[480]



$C_{11}H_{20}O_2$
184.14633 g/mol

Melting Point 34 – 35 °C, lit.[480] melting point not quoted **^{1}HNMR** ($CDCl_3$, 500MHz): δ 0.86 (9H, s, C(C<u>H</u>$_3$)$_3$), 0.97 – 2.41 (m, 9H), 5.15 (1H, br t, ^{3}J=2.2Hz, equatorial -C<u>H</u>OH) 8.08 (1H, s, -OCO<u>H</u>) **^{13}CNMR** ($CDCl_3$, 125.7MHz): δ 27.53 (-C(<u>C</u>H$_3$)$_3$), 73.59 (-<u>C</u>HOH), 160.74 (O<u>C</u>OH) **MS EI** *m/z* (%): 156 (10, M-HCO), 147 (30), 57 (100, $C_4H_9^+$)

1-_n_-Butyl-3-methylimidazolium Bromide 223[481]

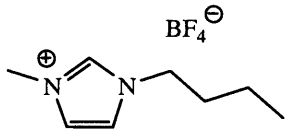


$C_8H_{15}BrN_2$
218.04186 g/mol

The *title compound* was prepared by a modified literature method.[481] To a stirred solution of N-methylimidazole (20.0 mL, 0.25 mol, 1.0 eq) in 1,1,1-trichloroethane (100 mL), freshly distilled *n*-bromobutane (16.0 mL, 0.30 mol, 1.2 eq) was added over 1 hour before the mixture was heated to reflux for 3 hours. After being cooled to room

temperature, the viscous product was decanted from the reaction solvent and was washed with ethyl acetate (25 mL x 5). The volatiles were removed by vigorous stirring *in-vacuo*, to yield the *title compound* as a light brown oil (50.2 g, 0.23 mol, 92%) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 0.98 (3H, t, ^{3}J=7.4Hz, $CH_2C\underline{H}_3$), 1.40 (2H, m, $C\underline{H}_2$), 1.96 (2H, m, $C\underline{H}_2$), 4.18 (3H, s, $C\underline{H}_3$), 4.42 (2H, t, ^{3}J=7.3Hz, $NC\underline{H}_2$), 7.83 (1H, t, ^{4}J=1.7Hz, $C\underline{H}$=CH), 7.89 (1H, t, ^{4}J=1.7Hz, $C\underline{H}$=CH), 10.23 (1H, m, N=C$\underline{H}$N) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 11.97 ($CH_2\underline{C}H_3$), 17.83 ($\underline{C}H_2$), 30.82 ($\underline{C}H_2$), 35.13 ($\underline{C}H_3$), 48.11 ($N\underline{C}H_2$), 121.03 ($\underline{C}$H=CH), 122.37 (CH=$\underline{C}$H), 135.24 (N=$\underline{C}$HN) **MS (FAB)** *M/z* (%): 139 (100, M^+-Br) **FTIR (ν_{max} cm^{-1})** neat 3436 (s, =NH), 3145 (s), 3072 (s), 2954 (s), 2863 (s), 1552 (s), 1488 (s), 798 (s), 624 (s)

1-*n*-Butyl-3-methylimidazolium tetrafluoroborate 224[482]



$C_8H_{15}BF_4N_2$
226.12644 g/mol

The *title compound* was prepared by a modified literature method.[482] 1-*n*-Butyl-3-methylimidazolium bromide **223** (25.1 g, 0.12 mol, 1.0 eq) was added to a suspension of $NaBF_4$ (15.2 g, 0.14 mol, 1.2 eq) in acetone (45 mL). The reaction was stirred at room temperature for 48 hours and then filtered to remove silver bromide. The filtrate was concentrated *in-vacuo*, diluted in DCM (75 mL) and filtered through silica gel (50 g) to remove traces of starting material. The DCM solution was washed with saturated Na_2CO_3 (30 mL x 2), dried and the volatiles were removed *in-vacuo* to yield the *title compound* as a brown oil (25.8 g, 0.11 mol, 95%) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 0.94 (3H, t, ^{3}J=7.4Hz, $CH_2C\underline{H}_3$), 1.36 (2H, m, $C\underline{H}_2$), 1.88 (2H, m, $C\underline{H}_2$), 3.96 (3H, s, $C\underline{H}_3$), 4.22 (2H, t, ^{3}J=7.4Hz, $NC\underline{H}_2$), 7.49 (2H, m, $C\underline{H}$=$C\underline{H}$), 8.72 (1H, m, N=C$\underline{H}$N) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 12.65 ($CH_2\underline{C}H_3$), 18.63 ($\underline{C}H_2$), 31.23 ($\underline{C}H_2$), 35.40 ($\underline{C}H_3$), 48.98 ($N\underline{C}H_2$), 121.88 ($\underline{C}$H=CH), 123.15 (CH=$\underline{C}$H), 135.36 (N=$\underline{C}$HN) **MS (FAB)** *M/z* (%): 139 (100, M^+-BF_4) **FTIR (ν_{max} cm^{-1})** neat 3162 (s), 2963 (s), 2876 (s), 1577 (s), 1468 (s), 1065 (s, B-F), 793 (s)

Oxidation general methods

Below are listed some of the key methods that were investigated when trying to determine suitable conditions for the oxidation of substrates using our ruthenium based complexes. Chapter 5 of this thesis discusses their development and demonstrates their effectiveness with a broad range of substrates.

Oppenauer type oxidation method A

Ruthenium complex (5.0 mol%) and K_2CO_3 (0.5 eq) were added to acetone (50 mL) for a 45-minute incubation period at reflux. The substrate alcohol (10.0 mmol) was then added and the reaction mixture maintained at reflux for 60 hours. The reaction was cooled to room temperature, filtered and the volatiles were removed *in-vacuo*. The residue was purified by column chromatography.

General method for NMO promoted oxidation

Molecular sieves (500 mg/mmol, finely ground), NMO (1.2 eq) and alcohol (10.0 mmol) were added to DCM (50 mL) at room temperature, followed by ruthenium complex (5 mol%). The reaction mixture was stirred under a N_2 atmosphere for 24 hours at room temperature. The reaction was filtered, the volatiles were removed *in-vacuo* and the residue purified by column chromatography.

General method for TMANO promoted oxidation

Molecular sieves (500 mg/mmol, finely ground), TMANO (1.2 eq) and alcohol (10.0 mmol) were added to DCM (50 mL) at room temperature, followed by ruthenium complex (5 mol%). The reaction mixture was stirred under a nitrogen atmosphere, for 24 hours at room temperature whilst a stream of N2 purged the solution. The reaction was filtered, the volatiles were removed *in-vacuo* and the residue purified by column chromatography.

General method for *Tert*-Butyl peroxide promoted oxidation

Tert-Butyl peroxide (4.0 eq) was added *via* syringe pump over 2 hours to a solution of alcohol (10.0 mmol) and ruthenium complex (5 mol%) in DCM (50 mL) at room temperature. The reaction mixture was stirred under a nitrogen atmosphere for 2 hours at room temperature, the volatiles were removed *in-vacuo* and the residue purified by column chromatography.

General method for TCCA promoted oxidation

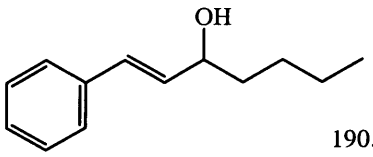
Ruthenium complex (1 mol%), tetrabutylammonium bromide (4.0 mol%), K_2CO_3 (3.0 eq), and alcohol (10.0 mmol) were added to EtOAc/Water (20 mL, 1:1 v/v). TCCA (0.7 eq) dissolved in EtOAc (10 mL) was added dropwise to the reaction solution, using cooling if necessary to maintain the temperature below 40 °C. The reaction was stirred at room temperature under ambient conditions for 1 hour, then propan-2-ol (1 mL) was added followed by stirring for 15 minutes to destroy the excess TCCA. The reaction was filtered, the aqueous layer separated and extracted with EtOAc. The combined organic fractions were washed with brine, dried and the volatiles removed *in-vacuo*. The residue was purified by column chromatography.

Oxidation products

All of the following compounds were analysed by ^{1}HNMR, ^{13}CNMR and where appropriate, melting point and were found to have identical spectral and physical properties to authentic samples.

Acetophenone	Benzaldehyde	4-Methylbenzaldehyde
4-Methoxybenzaldehyde	4-Chlorobenzaldehyde	4-Bromobenzaldehyde
4-Nitrobenzaldehyde	2-Methoxybenzaldehyde	2-Phenylacetylaldehyde
Cinnamaldehyde	Thiophene-2-carbaldehyde	1-Decanal
E-3,7-Dimethyl-octa-2,6-dienal[483]	*Z*-3,7-Dimethyl-octa-2,6-dienal[483]	2,2,2-trifluoroacetophenone
Benzil	*trans*-Menthone	4-*tert*-Butyl cyclohexanone
(*E*)-l-Phenyl-l-hepten-3-one	6-Undecanone	Benzoic acid
6-Methylbenzaldehyde	3-Bromobenzaldehyde	6-Bromobenzaldehyde
4-Methoxybenzoic acid	3-Phenylpropionaldehyde	2-Methoxy-5-bromo benzaldehyde
4-Nitrobenzoic acid		

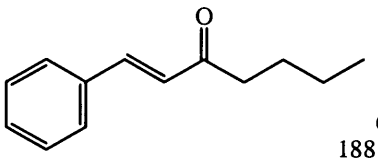
(*E*)-1-Phenyl-1-hepten-3-ol 252[484]



$C_{13}H_{18}O$
190.13577 g/mol

The *title compound* was prepared by a literature method.[484] A solution of *n*-BuLi (14.0 mL, 39.7 mmol, 2.86 M in hexane, 1.0 eq) was diluted with THF (20 mL), cooled to -78 °C, and treated dropwise with cinnamaldehyde (5.0 mL, 39.7 mmol, 1.0 eq). The solution was stirred at -78 °C for 30 minutes, warmed to room temperature and quenched with aqueous $NaHSO_4$ (10 mL). The reaction was diluted with ether (25 mL) and the aqueous layer was removed. The organic layer was washed with $NaHCO_3$ (10 mL x 2) and brine (10 mL), dried and the volatiles removed *in-vacuo*. The crude material was purified by column chromatography (4:1 petroleum spirit:ethyl acetate), to yield the product as a colourless oil (4.83 g, 25.4 mmol, 64%) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 0.81 (3H, t, ^{3}J=6.9Hz, C$\underline{H}_3$), 1.21 – 1.40 (4H, m, C$\underline{H}_2$), 1.43 – 1.62 (2H, m, C$\underline{H}_2$), 2.17 (1H, br s, O$\underline{H}$), 4.15 (1H, q, ^{3}J=6.6Hz, C$\underline{H}$OH), 6.12 (1H, dd, ^{3}J=15.9Hz, ^{4}J=6.6Hz, CH=C$\underline{H}$CHOH), 6.45 (1H, d, ^{3}J=15.9Hz, C$\underline{H}$=CHCHOH), 7.09 – 7.84 (5H, m, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 13.94 (C$\underline{H}_3$), 22.55 (C$\underline{H}_2$), 27.52 (C$\underline{H}_2$), 36.97 (C$\underline{H}_2$), 72.86 (C$\underline{H}$OH), 126.30 (ArC$\underline{H}$) 127.40 (C$\underline{=}$C) 128.41 (ArC$\underline{H}$), 129.90 (C=C$\underline{}$), 132.62 (ArC$\underline{H}$), 136.69 (ArC$\underline{_Q}$CH) **MS EI** *m/z* (%): 190 (M^+, 10), 133 (100), 105 (60), 91 (65) **FTIR (ν_{max} cm^{-1})** neat 3380 (br), 3076 (s), 3058 (s), 3031 (s), 2980 (s), 2935 (w), 1650 (s), 1565 (s), 1441 (s), 1353 (s), 1009 (s), 774 (s)

(*E*)-1-Phenyl-1-hepten-3-one 253[485]



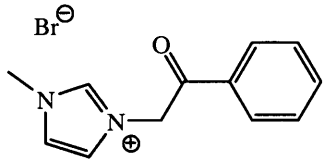
$C_{13}H_{16}O$
188.12012 g/mol

Melting Point 44 – 45 °C, lit.[485] 45 – 46 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 0.94 (3H, t, ^{3}J=7.3Hz, C$\underline{H}_3$), 1.37 (2H, quin, C$\underline{H}_2$), 1.67 (2H, m, C$\underline{H}_2$), 2.64 (2H, t, ^{3}J=7.6Hz, C$\underline{H}_2$), 6.75 (1H, d, ^{3}J=16.3Hz, C$\underline{H}$=CH), 7.32 (3H, m, ArC$\underline{H}$), 7.55 (1H, d, ^{3}J=16.3Hz,

CH=C*H*), 7.53 – 7.57 (3H, m, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 14.02 (*C*H_3), 22.48 (*C*H_2), 26.59 (*C*H_2), 40.86 (*C*H_2), 126.42 (Ar*C*H) 128.31 (Ar*C*H), 129.05 (Ar*C*H), 130.46 (*C*=C), 134.72 (C=*C*), 142.44 (Ar*C*$_Q$CH), 200.71 (Ar*C*$_Q$O) **MS EI** *m/z* (%): 131 (100), 103 (70), 77 (45) **FTIR (ν_{max} cm^{-1})** nujol 3020 (s), 1689 (s), 1620 (s, C=O), 1606 (s), 1570 (s), 1504 (s), 1449 (s), 1408 (s), 1009 (s), 796 (s)

Novel ACAC mimic Ligands

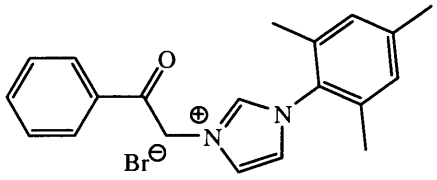
1-methyl-3-phenacyl-imidazolium bromide 278[486,491]



$C_{12}H_{13}BrN_2O$
280.02113 g/mol

The *title compound* was prepared by a literature method.[491] 1-Methylimidazole (0.37 mL, 4.6 mmol, 1.0 eq) was added to a solution of 2-bromoacetophenone (0.91 g, 4.6 mmol, 1.0 eq) in THF (20 mL) and stirred at room temperature for 5 minutes. The white solid was broken up and washed with ether (10 mL x 2) before being dried *in-vacuo* to give the *title compound* (1.21 g, 4.3 mmol, 94%) **Melting Point** 150 – 151 °C, lit.[486] 153 – 155 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 3.97 (3H, s, C*H*$_3$), 6.22 (2H, s, C*H*$_2$), 7.62 (2H, m, ArC*H*), 7.76 (1H, m, ArC*H*), 7.84 (2H, m, ArC*H*), 8.06 (2H, m, *H*C=C*H*) 9.24 (1H, s, $^+$N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 36.31 (*C*H_3), 55.80 (*C*H_2), 123.52 (Ar*C*H), 124.12 (Ar*C*H), 128.46 (Ar*C*H), 129.35 (Ar*C*H), 133.86 (Ar*C*H), 134.77 (Ar*C*$_Q$), 137.93 (N$^+$=*C*HN), 191.70 (*C*$_Q$O) **HRMS (FAB)** *m/z* (%): ($C_{12}H_{13}BrN_2O$ - Br) Requires 202.11061 (M^+H-Br), Found: 202.11100 (30, M^+H-Br), 201 (100, M^+-Br) **FTIR (ν_{max} cm^{-1}) KBr** 3465 (br, =NH) 3080 (s), 2955 (s, CH_3), 2039 (w), 1709 (s, CO), 789 (s), 1164 (s), 1229 (s)

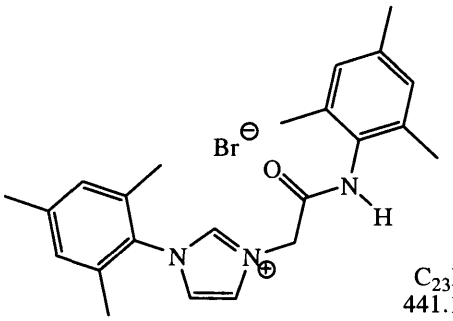
1-mesityl-3-phenacyl-imidazolum bromide 279



$C_{20}H_{21}BrN_2O$
384.08373 g/mol

The *title compound* was synthesised by the dropwise addition of 2-bromoacetophenone (530 mg, 2.7 mmol, 1.0 eq) in acetonitrile (2 mL) to mesityl imidazole **96** (500 mg, 2.7 mmol, 1.0 eq) in acetonitrile (5 mL) at room temperature. On completion of the addition, the reaction was stirred for 12 hours at room temperature, before the volatiles were removed *in-vacuo*. The crude white compound was washed with ether, then petroleum spirit to give the *title compound* as a white solid (940 mg, 2.4 mmol, 89%). **Melting Point** 185 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.08 (6H, s, *o*-ArC$\underline{H}_3$), 2.32 (3H, s, *p*-ArC$\underline{H}_3$), 6.72 (2H, s, -C$\underline{H}_2$-), 6.98 (2H, s, *m*-ArC$\underline{H}$), 7.15 (1H, t, ^{4}J=1.7Hz, Imidazole C$_{4/5}\underline{H}$), 7.47 (2H, m, ArC$\underline{H}$), 7.59 (1H, tt, ^{3}J=7.4Hz, ^{4}J=1.1Hz, ArC$\underline{H}$), 7.96 (1H, t, ^{4}J=1.5Hz, Imidazole C$_{4/5}\underline{H}$), 8.09 (2H, dd, ^{3}J=7.2, ^{4}J=1.3Hz, ArC$\underline{H}$), 9.83 (1H, t, ^{4}J=1.4, Imidazole C$_1\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 17.51 (*p*-Ar$\underline{C}$H$_3$), 21.05 (*o*-Ar$\underline{C}$H$_3$), 56.36 (-C$\underline{H}_2$-), 122.03 (Ar$\underline{C}$H), 124.93 (Ar$\underline{C}$H), 128.66 (Ar$\underline{C}$H), 129.07 (Ar$\underline{C}$H), 129.73 (Ar$\underline{C}$H), 130.55 (Ar$\underline{C}_Q$), 133.48 (Ar$\underline{C}_Q$), 134.34 (Ar$\underline{C}_Q$), 134.59 (Ar$\underline{C}$H), 138.80 (Ar$\underline{C}$H), 141.30 (Ar$\underline{C}_Q$), 190.76 (Ar$\underline{C}_Q$O) **HRMS (FAB)** *m/z* (%): ($C_{20}H_{21}BrN_2O$ +H-Br) Requires 306.17320 (M^+H-Br), Found: 306.17096 (75, M^+H-Br) **FTIR (ν_{max} cm^{-1})** KBr 3075 (s, =NH), 3015 (s), 2965 (s), 1714 (s, CO), 1454 (br), 1239 (s), 1205 (s), 779 (s)

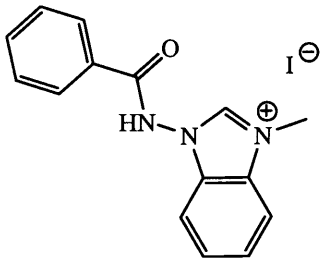
1-(2,4,6-trimethylphenyl)-3-(2,4,6-trimethylphenylacetimido)-imidazolium bromide 280



$C_{23}H_{28}BrN_3O$
441.14158 g/mol

The *title compound* was synthesised by the addition of 2-bromo-*N*-(2,4,6-trimethylphenyl)acetamide **380** (0.57 g, 2.68 mmol, 1.0 eq) diluted in acetonitrile (2 mL) to a refluxing solution of mesityl imidazole **96** (0.50 g, 2.68 mmol, 1.0 eq) in acetonitrile (5 mL). The reaction solution was maintained at reflux for 10 hours, cooled to room temperature and diethyl ether added to precipitate the product, which was separated from the reaction solution *via* filtration. The crude product was washed with diethyl ether, then petroleum spirit and dried *in-vacuo* to give the *title compound* as white needles (1.10 g, 2.49 mmol, 93%). **Melting Point** >220 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 2.00 (6H, s, *o*-ArC$\underline{H}_3$), 2.12 (6H, s, *o*-ArC$\underline{H}_3$), 2.19 (3H, s, *p*-ArC$\underline{H}_3$), 2.30 (3H, s, *p*-ArC$\underline{H}_3$), 5.41 (2H, s, C$\underline{H}_2$), 6.86 (2H, s, ArC$\underline{H}$), 7.12 (2H, s, ArC$\underline{H}$), 7.92 (1H, dd, ^{3}J=1.7Hz, -$\underline{H}$C=CH-), 8.09 (1H, dd, ^{3}J=1.7Hz, -HC=C$\underline{H}$-), 9.52 (1H, dd, ^{4}J=1.4Hz, N=C$\underline{H}$N)), 9.93 (1H, s, N$\underline{H}$) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 15.64 (*p*-Ar$\underline{C}$H$_3$), 16.91 (*p*-Ar$\underline{C}$H$_3$), 19.29 (*o*-Ar$\underline{C}$H$_3$), 19.41 (*o*-Ar$\underline{C}$H$_3$), 49.85 (C$\underline{H}_2$), 122.01 (Ar$\underline{C}$H), 123.35 (Ar$\underline{C}$H), 127.14 (Ar$\underline{C}$H), 128.03 (Ar$\underline{C}$H), 129.94 (ArC_Q), 130.25 (ArC_Q), 133.08 (ArC_Q), 133.58 (ArC_Q), 134.64 (ArC_Q), 137.84 (Ar$\underline{C}$H), 139.04 (ArC_Q), 162.67 (ArC_QO) **MS (ES)** *m/z* (%): 362 (100, M^+-Br) **FTIR (ν_{max} cm^{-1})** KBr 3450 (br, NH), 3175 (s), 3015 (s), 2945 (s), 1699 (s, CO), 1539 (s), 1269 (s), 1219 (s), 754 9w) **Elemental analysis** Calculated C 62.44%, H 6.38%, N 9.50%; Found C 62.12%, H 6.42%, N 9.22%

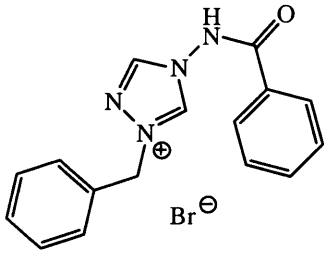
1-Phenacetylamino-3-methyl-benzimidazolium Iodide 281[487]



$C_{15}H_{14}IN_3O$
379.01816 g/mol

The *title compound* was synthesised by the addition of benzoyl chloride (0.39 mL, 3.4 mmol, 1.0 eq) to a refluxing mixture of 1-amino-3-methylbenzimidazolium iodide, **382** (0.92 g, 3.4 mmol, 1.0 eq), DMAP (41 mg, 0.34 mmol, 0.1 eq) and K_2CO_3 (0.47 g, 3.4 mmol, 1.0 eq) in acetonitrile (10 mL). The reaction was maintained at reflux for 4 hours with a gradual progression of colour from yellow to red observed. The reaction was filtered whilst hot and the filtrate was allowed to cool to room temperature. The product precipitated and was collected *via* filtration, washed with cold acetonitrile and dried *in-vacuo* to give the *title compound* as a white solid (1.25 g, 3.3 mmol, 97%). **Melting Point** 183 °C, lit.[487] 180 – 181 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 4.21 (-C*H*$_3$), 7.61 (2H, m, ArC*H*), 7.73 (3H, m, ArC*H*), 7.88 (1H, m, ArC*H*), 8.12 (1H, m, ArC*H*), 8.22 (1H, m, ArC*H*), 10.33 (1H, s, N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 33.96 (*C*H$_3$), 112.79 (Ar*C*H), 113.70 (Ar*C*H), 114.19 (Ar*C*H), 127.16 (Ar*C*H), 127.66 (Ar*C*H), 128.51 (Ar*C*H), 128.90 (Ar*C*H), 130.08 (ArC_Q), 130.47 (ArC_Q), 130.86 (ArC_Q), 133.49 (Ar*C*H), 166.16(ArC_Q) **HRMS (ES)** *m/z* (%): ($C_{15}H_{14}IN_3O$ -I) Requires 252.11314, Found: 252.11301 (95, M^+-I) **FTIR (ν_{max} cm^{-1})** KBr 3330 (s), 3105 (s), 3025 (br), 2935 (br), 2870 (br), 1679 (CO, s), 1569 (s), 1474 (s), 1278 (s), 894 (s)

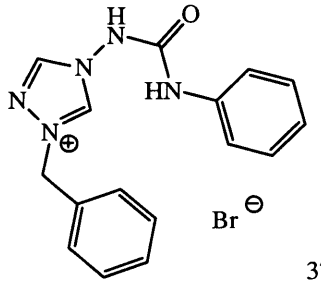
1-Phenacetylamino-3-benzyl-1,2,4-triazolium bromide 282[488]



$C_{16}H_{15}BrN_4O$
358.04292 g/mol

The *title compound* was synthesised by addition of benzyl bromide (1.20 mL, 10.0 mmol, 1.0 eq) to a refluxing solution of **383**, (1.88 g, 10.0 mmol, 1.0 eq) in acetonitrile (10 mL). The reaction was stirred at reflux for 6 hours, before being cooled to room temperature, which resulted in the formation of a precipitate. The precipitate was collected *via* filtration, washed with EtOAc (25 mL x 2) and dried *in vacuo* to give the *title compound* as a white solid (2.94 g, 8.2 mmol, 82%). **Melting Point** 190 °C, lit.[488] 188 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.73 (2H, s, CH_2), 7.06 (1H, t, ^{3}J=7.4Hz, ArC*H*), 7.33 (2H, t, ^{3}J=7.9Hz, ArC*H*), 7.48 (7H, m, ArC*H*), 10.12 (1H, br s, N=C*H*N), 10.58 (1H, br s, N*H*), 10.85 (1H, d, ^{4}J=2.7Hz $^+$N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 118.91 (Ar*C*H), 122.75 (Ar*C*H), 128.85 (Ar*C*H), 138.93 (ArC_Q), 144.66 (Ar*C*H), 168.93 (ArC_QO) **HRMS (EI)** *m/z* (%): ($C_{16}H_{15}BrN_4O$ +H-Br) Requires 238.09749 (M^+H-Br), Found: 238.09770 (100, M^+H-Br), 134 (30, $C_7H_6N_2O$) **FTIR (ν_{max} cm^{-1}) KBr** 3255 (s), 3195 (s), 3135 (s), 3085 (s), 2915 (br), 1959 (w), 1744 (CO, s), 1684 (s), 1549 (s), 1334 (s), 1074 (s), 894 (s)

1-phenyl-3-(1-benzyl-1,2,4-triazolium)-urea bromide 283[489]

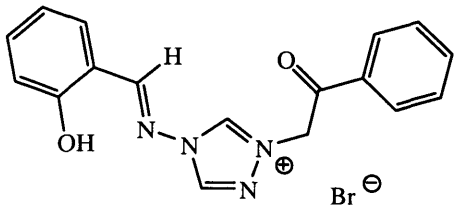


$C_{16}H_{16}BrN_5O$
373.05382 g/mol

The *title compound* was synthesised by dissolving **384**, (2.03 g, 10.0 mmol, 1.0 eq) in DMF (3 mL) and diluting further with ethanol (25 mL, 99.6%). The solution was

heated to reflux and benzyl bromide (1.20 mL, 10.0 mmol, 1.0 eq) added. The reaction was stirred at reflux for 5 hours, before cooling to room temperature and collection of the precipitate *via* filtration. The precipitate was washed with EtOAc (25 mL x 2) and dried *in vacuo* to yield the *title compound* as a white solid (3.35 g, 9.0 mmol, 90%). **Melting Point** 219 – 220 °C, lit.[489] 221 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.75 (2H, s, CH_2), 7.06 (1H, t, ^{3}J=7.4Hz, ArC*H*), 7.32 (2H, t, ^{3}J=7.9Hz, ArC*H*), 7.48 (7H, m, ArC*H*), 9.61 (1H, s, N=C*H*N), 10.18 (1H, s, N*H*), 10.59 (1H, s, N*H*), 10.91 (1H, s, $^+$N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 55.34 (*C*H_2) 118.93 (Ar*C*H), 123.32 (Ar*C*H), 128.92 (Ar*C*H), 128.97 (multiple Ar*C*H), 129.09 (Ar*C*H), 132.94 (ArC_Q), 138.09 (Ar*C*H), 138.21 (ArC_Q) 152.94 (ArC_QO) **HRMS (EI)** *m/z* (%): ($C_{16}H_{16}BrN_5O$ +H-Br) Requires 294.13494 (M^+H-Br) Found: 294.13447 (100, M^+H-Br) **FTIR (ν_{max} cm^{-1})** KBr 3471 (br), 3259 (s), 3194 (s), 3122 (s), 3074 (s), 3054 (s), 2936 (s), 1723 (CO, s), 1569 (s), 1331 (s), 1078 (s), 768 (s)

4-[(2-Hydroxy-benzylidine)-amino]-1-phenacyl-(1,2,4-triazolium) bromide 284

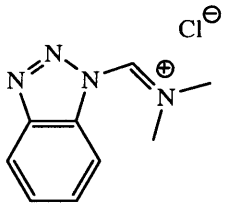


$C_{17}H_{15}BrN_4O_2$
386.03784 g/mol

The *title compound* was synthesised by the condensation of **385**, (1.00 g, 3.55 mmol, 1.0 eq) with salicaldehyde (400 µl, 3.55 mmol, 1.0 eq) in refluxing acetonitrile (10 mL) over a period of 6 hours. The reaction was cooled to room temperature, the volatiles were removed *in-vacuo* and the solid washed with ether. Recrystallisation of the solid from ethanol/ether resulted in the *title compound* being isolated as a white solid (315 mg, 0.82 mmol, 23%). **Melting Point** >220 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 6.43 (2H, s, -CH_2-), 6.99 (1H, dd, ^{3}J=7.6Hz, ArC*H*), 7.09 (1H, d, ^{3}J=8.3, ArC*H*), 7.51 (1H, dt, ^{3}J=6.9Hz, ^{4}J=1.6Hz, ArC*H*), 7.64 (2H, dd, ^{3}J=7.7Hz, ArC*H*), 7.78 (1H, t, ^{3}J=7.4Hz, ArC*H*), 7.90 (1H, dd, ^{3}J=7.8Hz, ^{4}J=1.2Hz, ArC*H*), 8.12 (2H, d, ^{3}J=7.4Hz, ArC*H*), 9.40 (1H, s, -N-C*H*=N-), 10.03 (1H, s, N=C*H*), 10.79 (1H, br s, O*H*), 10.85 (1H, s, -N-C*H*=N$^+$-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 58.06 (-CH_2-), 112.32 (Ar*C*H), 113.61

(Ar<u>C</u>H), 116.92 (Ar<u>C</u>H), 116.99 (Ar<u>C</u>H), 119.75 (Ar<u>C</u>H), 127.56 (Ar<u>C</u>H), 128.43 (Ar<u>C</u>H), 129.06 (Ar<u>C</u>H), 133.30 (Ar<u>C</u>$_Q$OH), 134.76 (Ar<u>C</u>H), 135.69 (-N=<u>C</u>H-), 159.36 (Ar<u>C</u>$_Q$C=N-), 161.78 (Ar<u>C</u>H), 190.06 (<u>C</u>$_Q$O) **HRMS (EI)** *m/z* (%): ($C_{17}H_{15}BrN_4O_2$ -Br) Requires 307.11895 (M^+-Br), Found: 307.11841 (95, M^+-Br) **FTIR (ν_{max} cm^{-1})** KBr 3259 (br, NH), 3159 (s), 3128 (s), 3041 (br), 2921 (s), 2961 (s), 1681 (CO, s), 1525 (s), 1354 (s), 1239 (s), 764 (s), 619 (s)

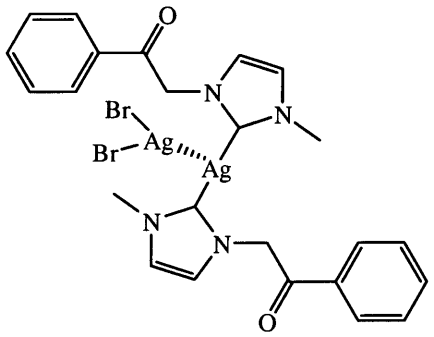
Benzotriazole-*N*-methyleniminium chloride 285[490]



$C_9H_{11}ClN_4$
210.06722 g/mol

The *title compound* was prepared by a literature method.[490] DMF (1.96 mL, 25.0 mmol, 1.0 eq) and triphenylphosphine (6.55 g, 25.0 mmol, 1.0 eq) were added to THF (25 mL) and 1-Chlorobenzatriazole **386** (3.81 g, 25.0 mmol, 1.0 eq) in THF (10 mL) was added dropwise to the reaction solution. On completion of the addition, the reaction mixture was refluxed for 3 hours, cooled, filtered, and the precipitate collected. The solid was washed with THF to give the *title compound* as a white deliquescent solid (3.90 g, 18.7 mmol, 74%) **Melting Point** 108 –109 °C, lit.[490] value not given **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.88 (3H, s, N(C<u>H</u>$_3$)), 2.96 (3H, s, N(C<u>H</u>$_3$)), 7.55 (2H, dd, ^{3}J=9.5Hz, ^{4}J=3.1Hz, ArC<u>H</u>), 8.01 (2H, dd, ^{3}J=9.5Hz, ^{4}J=3.1Hz, ArC<u>H</u>) 8.04 (1H, br s, -NC<u>H</u>=N) **^{13}CNMR** ($CDCl_3$,, 75.5MHz): δ 42.00 (N<u>C</u>H$_3$), 47.55 (N<u>C</u>H$_3$), 114.37 (Ar<u>C</u>H), 120.28 (Ar<u>C</u>H), 126.86 (Ar<u>C</u>H), 128.74 (Ar<u>C</u>H), 130.65 (Ar<u>C</u>$_Q$), 146.29 (Ar<u>C</u>$_Q$) 152.86 (N=<u>C</u>H) **MS (FAB)** *m/z* (%): 348 (10, dimer), 176 (100, M^+-Cl) **FTIR (ν_{max} cm^{-1})** KBr 3360 (br), 3092 (w), 3047 (w), 2505 (br), 1963 (br), 1620 (s), 1526 (w), 1417 (s), 1292 (s), 1248 (s), 1128 (s), 1009 (s), 890 (s)

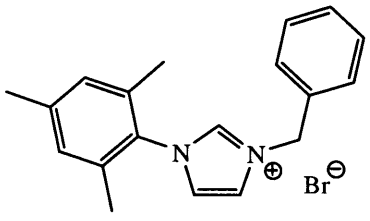
[Ag(3-methyl-1-phenacylimidazolin-2-ylidene)$_2$][Ag-Br$_2$] 286[491]



$C_{24}H_{26}Ag_2Br_2N_4O_2$
773.85244 g/mol

The *title compound* was prepared by a literature method.[491] 1-Phenyl-3-(aceto-2-phenone)-imidazolium bromide **278** (1.11 g, 3.95 mmol, 1.0 eq) was stirred with freshly prepared Ag_2O (0.46 g, 1.98 mmol, 0.5 eq) in DCM (100 mL) at room temperature for 2 hours. The reaction mixture was filtered under nitrogen, through celite, and the filtrate collected. The volatiles were removed *in-vacuo*, the solid washed with ether (10 mL x 2) and dried *in-vacuo* to give the *title compound* as an orange solid (300 mg, 0.39 mmol, 20%) The melting point and FTIR of this compound were not recorded due to its instability. **^{1}HNMR** (DMSO-D_6, 300MHz): δ 3.76 (6H, s, C$\underline{H}_3$), 5.89 (4H, s, C$\underline{H}_2$), 7.54 (4H, m, ArC$\underline{H}$), 7.68 (2H, m, ArC$\underline{H}$), 7.81 (4H, m, ArC$\underline{H}$), 8.01 (1H, m, $\underline{H}$C=CH) 8.05 (1H, m, HC=C$\underline{H}$) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 38.52 ($\underline{C}H_3$), 57.26 ($\underline{C}H_2$), 122.74 (Ar$\underline{C}$H), 123.65 (Ar$\underline{C}$H), 128.21 (Ar$\underline{C}$H), 129.09 (Ar$\underline{C}$H), 134.33 (Ar$\underline{C}$H), 134.51 (Ar$\underline{C}_Q$), 182.36 ($\underline{C}_Q$O), 193.41 ($\underline{C}_{Carbene}$) **X-Ray** see appendix

1-Mesityl-3-benzylimidazolium bromide 287



$C_{19}H_{21}BrN_2$
356.08881 g/mol

The *title compound* was synthesised by addition of benzyl bromide (0.32 mL, 2.68 mmol, 1.0 eq) in acetonitrile (1 mL) to a refluxing solution of mesityl imidazole **96** (500 mg, 2.68 mmol, 1.0 eq) in acetonitrile (10 mL). The reaction was maintained at reflux

for 3 hours, before being cooled to room temperature, which resulted in the precipitation. The precipitate was collected *via* filtration, washed with ether and dried *in-vacuo* to give the *title compound* as a white solid (0.92 g, 2.57 mmol, 96%). **Melting Point** >220 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 2.02 (6H, s, *o*-ArC$\underline{H}_3$), 2.32 (3H, s, *p*-ArC$\underline{H}_3$), 5.64 (2H, s, C$\underline{H}_2$), 7.15 (2H, s, ArC$\underline{H}$), 7.43 (3H, m, ArC$\underline{H}$), 7.54 (2H, m, ArC$\underline{H}$), 8.00 (1H, m, -$\underline{H}$C=CH-), 8.19 (1H, m, -HC=C$\underline{H}$-), 9.90 (1H, s, N=C$\underline{H}$N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 16.97 (*o*-Ar$\underline{C}$H$_3$), 20.59 (*p*-Ar$\underline{C}$H$_3$), 52.10 ($\underline{C}$H$_2$), 123.17 (Ar$\underline{C}$H), 124.21 (Ar$\underline{C}$H), 128.20 (Ar$\underline{C}$H), 128.77 (Ar$\underline{C}$H), 129.03 (Ar$\underline{C}$H), 129.25 (Ar$\underline{C}$H), 131.10 (Ar$\underline{C}_Q$), 134.18 (*o*-Ar$\underline{C}_Q$CH$_3$), 134.86 (*p*-Ar$\underline{C}_Q$CH$_3$), 140.21 (Ar$\underline{C}_Q$) **HRMS (FAB)** *m/z* (%): ($C_{19}H_{21}BrN_2$ +H-Br) Requires 278.17829 (M^+H-Br) Found: 278.17841 (100, M^+H-Br) **FTIR (ν_{max} cm^{-1})** KBr 3430 (br), 3150 (s, =NH), 3105 (s), 3065 (s), 3000 (br), 2940 (s), 2430 (w), 1544 (s), 1089 (s), 724 (w) **Elemental analysis** Calculated C 62.35%, H 5.49%, N 7.27%; Found C 62.34%, H 5.66%, N 6.88%

Heck reactions

Below are listed some of the key methods which were investigated when attempting to determine suitable conditions for Heck coupling using our novel range of ligands. Chapter 6 of this thesis discusses their development and demonstrates their effectiveness.

Pd (0) catalysed Heck reaction method A

$Pd(dba)_2$ (1.0 mol%), imidazolium salt (1.0 mol%) and Cs_2CO_3 (2.0 eq) were added to DMAC (2 mL), and stirred at room temperature for 30 minutes. Following this, a simultaneous addition of bromobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made, and the reaction mixture heated to 120 °C for 2 hours. The reaction was cooled, diluted with ether (10 mL) and filtered through a plug of silica. The volatiles were removed *in-vacuo* and the residue purified by column chromatography.

Pd (0) catalysed Heck reaction method B

$Pd(dba)_2$ (1.0 mol%), imidazolium salt (1.0 mol%) and Cs_2CO_3 (2.0 eq) were added to dioxane (2 mL), and stirred at room temperature for 30 minutes. Following this, a simultaneous addition of bromobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made,

and the reaction mixture heated to 80 °C for 12 hours. The reaction was cooled, diluted with ether (10 mL) and filtered through a plug of silica. The volatiles were removed *in-vacuo* and the residue purified by column chromatography.

Pd (II) catalysed Heck reaction method A

$Pd(OAc)_2$ (2.5 mol%), imidazolium salt (2.5 mol%) and Cs_2CO_3 (2.0 eq) were added to dioxane or DMAC (2 mL), and stirred at 90 °C for 30 minutes. Following this, a simultaneous addition of bromobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made, and the reaction mixture heated to 90 °C for 12 hours. The reaction was cooled, diluted with ether (10 mL) and filtered through a plug of silica. The volatiles were removed *in-vacuo* and the residue purified by column chromatography.

Pd (II) catalysed Heck reaction method B

$PdCl_2(PPh_3)_2$ (2.5 mol%), imidazolium salt (2.5 mol%) and Cs_2CO_3 (2.0 eq) were added to dioxane (2 mL), and stirred at 90 °C for 30 minutes. Following this, a simultaneous addition of bromobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made, and the reaction mixture heated to 90 °C for 12 hours. The reaction was cooled, diluted with ether (10 mL) and filtered through a plug of silica. The volatiles were removed *in-vacuo* and the residue purified by column chromatography.

Pd (II) catalysed Heck reaction method C

$PdCl_2(PPh_3)_2$ (2.5 mol%), imidazolium salt (2.5 mol%) and Cs_2CO_3 (2.0 eq) were added to DMAC (2 mL), and stirred at 90 °C for 30 minutes. Following this, a simultaneous addition of bromobenzene (1.0 eq) and ethyl acrylate (1.5 eq) was made, and the reaction mixture heated to 90 °C for 12 hours. The reaction was cooled, diluted with ether (10 mL) and filtered through a plug of silica. The volatiles were removed *in-vacuo* and the residue purified by column chromatography.

Heck products

The compounds synthesised by Heck coupling were analysed by ^{1}HNMR, ^{13}CNMR and where appropriate, melting point and were found to have identical spectral and physical properties to authentic samples

trans-Ethyl cinnamate 288

trans-Cinnamic acid 289

Suzuki reactions

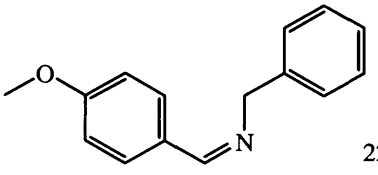
The following general method was used to investigate the activity of our novel ligand range for the palladium catalysed Suzuki reaction. Chapter 6 of this thesis discusses its development and demonstrates its effectiveness.

Pd (0) catalysed Suzuki reaction

4-Chlorotoluene **290** (10.0 mmol), phenylboronic acid (1.0 eq), $Pd(dba)_2$ (0.03 eq), ligand (0.03 eq), KOMe (3.0 eq), and TBAB (0.1 eq) were combined in toluene (10 mL) at 40 °C for 12 hours. The reaction was cooled to room temperature, washed with HCl (5 mL, 2M), brine and filtered. The volatiles were removed *in-vacuo* and the residue purified by column chromatography, and the product, 4-Phenyl toluene **291**, was found to have identical spectral and physical properties to authentic samples

Nickel catalysed Transfer Hydrogenation

Benzylidine-(4-methoxy-phenyl)-amine 296[492]



$C_{15}H_{15}NO$
225.11536 g/mol

The *title compound* was synthesised by addition of benzyl amine (5.0 mL, 21.0 mmol, 1.0 eq) to a solution of 4-methoxy benzaldehyde (2.6 mL, 21.0 mmol, 1.0 eq) in ethanol (20 mL, 99.6%). The reaction was heated to reflux and stirred for 5 hours, cooled to room temperature and the volatiles removed *in-vacuo* to yield a pale yellow oil. Trituration with pentane gave the *title compound* as a pale yellow powder (4.4 g, 19.7

r(3H, s, OC$\underline{H}_3$), 4.75 (2H, s, ArC$\underline{H}_2$), 6.88 (2H, d, ^{3}J=8.7Hz, ArC$\underline{H}$), 7.22 (1H, m, *p*-
(3H, s, OC$\underline{H}_3$), 4.75 (2H, s, ArC$\underline{H}_2$), 6.88 (2H, d, ^{3}J=8.7Hz, ArC$\underline{H}$), 7.22 (1H, m, *p*-

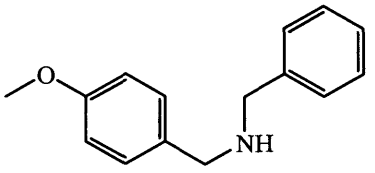
ArC*H*), 7.29 (4H, br d, ^{3}J=4.0Hz, ArC*H*), 7.69 (2H, d, ^{3}J=8.7Hz, ArC*H*), 8.28 (1H, br s, ArC*H*), 7.29 (4H, br d, ^{3}J=4.0Hz, ArC*H*), 7.69 (2H, d, ^{3}J=8.7Hz, ArC*H*), 8.28 (1H, br s, N=C*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 55.27 (O*C*H$_3$), 64.89 (Ar*C*H$_2$), 113.90 Ar*C*H), 126.82 (Ar*C*H), 127.87 (Ar*C*H), 128.38 (Ar*C*H), 129.07 (Ar*C*$_Q$CH=N), 129.76 (Ar*C*H), 139.51 (Ar*C*$_Q$CH$_2$), 161.21 (=N*C*H), 161.63 (Ar*C*$_Q$OCH$_3$) **MS EI** *m/z* (%): 225 (70, M$^+$), 134 (20), 91 (100) **FTIR** (**ν_{max} cm^{-1}**) KBr 3029 (w), 2954 (w), 2945 (w), 2845 (s), 2826 (s) 1648 (s), 1617 (s), 1245 (s), 1032 (s), 831 (s), 756 (s)

The following general method was used to investigate the activity of our novel ligand range for the nickel catalysed transfer hydrogenation of imines. Chapter 6 of this thesis discusses its development and demonstrates its effectiveness.

Nickel catalysed transfer hydrogenation of imines

Ligand (10 mol%) was added to Ni(acac)$_2$ (10 mol%) and NaH (3.6 eq) in dioxane (12 mL) at 100 °C and stirred for a 15-minute incubation period. After this pentan-3-ol (3.6 eq) was added dropwise and the reaction heated for 30 minutes. Imine (10.0 mmol) in dioxane (6 mL) was added dropwise and the reaction maintained at 100 °C for 12 hours, before cooling to room temperature. The volatiles were removed *in-vacuo* and the residue purified by column chromatography to give the reduced imine as product.

***N*-(4-methoxybenzyl)-phenylamine 297**[493]



$C_{15}H_{17}NO$
227.13101 g/mol

^{1}HNMR ($CDCl_3$, 300MHz): δ 3.74 (2H, s, ArC*H*$_2$), 3.85 (5H, br s, ArC*H*$_2$ + OC*H*$_3$), 6.91 (2H, d, ^{3}J=8.3Hz, ArC*H*), 7.29 (3H, m, ArC*H*), 7.37 (4H, m, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 52.44 (O*C*H$_3$), 52.99 (Ar-*C*H$_2$), 55.11 (Ar-*C*H$_2$), 113.71 (Ar*C*H), 126.85 (Ar*C*H), 128.11 (Ar*C*H), 128.36 (Ar*C*H), 129.18 (Ar*C*H), 132.41 (Ar*C*$_Q$CH$_2$), 140.33 (Ar*C*$_Q$CH$_2$), 158.56 (Ar*C*$_Q$OCH$_3$) **MS EI** *m/z* (%) 121 (40), 91 (100) **FTIR** (**ν_{max} cm^{-1}**) KBr 3329 (s), 2911 (w), 2835 (s), 1620 (s), 1501 (s), 1441 (s), 1282 (s), 1231 (s), 1156 (s) , 818 (s)

Dehalogenation

The following general method was used to investigate the activity of our novel ligand range for the nickel catalysed dechlorination of arenes. Chapter 6 of this thesis discusses its development and demonstrates its effectiveness.

Nickel catalysed dehalogenation of aryl halides

$Ni(acac)_2$ (3 mol%), NaH (3.1 eq), and ligand (6 mol%) were added to THF (6 mL) and heated to reflux. Propan-2-ol (3.0 eq) was added dropwise to the reaction solution, which was maintained at reflux for 1 hour as an incubation period. Aryl chloride (10.0 mmol) in THF (3 mL) was added and the reaction stirred for 12 hours under reflux, before being cooled to room temperature. Water (2 mL) was added to the reaction, the volatiles were removed *in-vacuo*, the residue extracted with ether and purified by column chromatography.

The product ***tert*-Butyl benzene 294** was found to have identical spectral and physical properties to an authentic sample.

Kumada coupling

The following general method was used to investigate the activity of our novel ligand range for the nickel catalysed dechlorination of arenes. Chapter 6 of this thesis discusses its development and demonstrates its effectiveness.

Palladium catalysed Kumada coupling method A

An addition of aryl halide (10.0 mmol) and phenylmagnesium bromide (1.0 M in THF, 1.5 eq) was made to a solution of ligand (4 mol%) and $Pd(OAc)_2$ (4 mol%) in dioxane (5 mL). The reaction was heated to 80 °C for 1 hour, cooled to room temperature and HCl (2 mL, 2 M) added. The reaction solution was extracted with ether (10 mL x 3) and the combined extracts washed with brine (5 mL). The organic extracts were dried, filtered and the volatiles removed *in-vacuo*. The residue was purified by column chromatography.

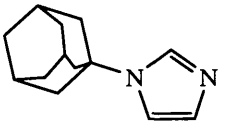
Palladium catalysed Kumada coupling method B

An addition of aryl halide (10.0 mmol) and phenylmagnesium bromide (1.0 M in THF, 1.5 eq) was made to a solution of ligand (4 mol%) and $Pd_2(dba)_3$ (4 mol%) in dioxane (5 mL). The reaction was heated to 80 °C for 1 hour, cooled to room temperature and HCl (2 mL, 2 M) added. The reaction solution was extracted with ether (10 mL x 3) and the combined extracts washed with brine (5 mL). The organic extracts were dried, filtered and the volatiles removed *in-vacuo*. The residue was purified by column chromatography.

The product, 1-Phenylheptane **304**, was found to have identical spectral and physical properties to an authentic sample.

Hydroacylation

1-Adamantylimidazole 307[494]

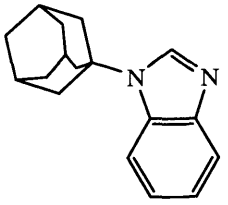


$C_{13}H_{18}N_2$
202.14700 g/mol

The *title compound* was prepared by a literature method.[494] Imidazole (4.74 g, 69.7 mmol, 5.0 eq) was heated to 80 °C in the presence of 1,2-dichlorobenzene (0.3 mL). 1-bromoadamantane (3.0 g, 14.0 mmol, 1.0 eq) was added to the melt and the reaction mixture was heated to 110 °C for 6 hours, before being cooled to room temperature. The excess imidazole was removed from the crude product *via* distillation *in vacuo* with the aid of a Bunsen burner, and the resulting residue was dissolved in chloroform (25 mL). The organic phase was washed with an aqueous solution of sodium acetate (2.30 g, 28.0 mmol, 2.0 eq), and then with water (3 x 30 mL), which removed all traces of imidazole. The organic phase was dried with anhydrous sodium sulphate, filtered and the solvent removed *in vacuo*. The residue obtained was stirred vigorously with hexane (30 mL) to precipitate 4-(1-adamantyl)-imidazole that was removed *via* filtration. The mother liquor was concentrated to dryness to yield the *title compound* as a cream solid (1.31g, 6.5 mmol, 46%). **Melting Point** 106 – 108 °C, lit.[494] 106 – 111 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.75 (6H, br s, -C<u>H</u>$_2$), 2.06 (6H, br s, -C<u>H</u>$_2$), 2.21 (3H, m, -C<u>H</u>),

7.03 (1H, dd, ^{4}J=1.2Hz, imidazole $C_{4/5}\underline{H}$), 7.05 (1H, dd, ^{4}J=1.4Hz, imidazole $C_{4/5}\underline{H}$), 7.62 (1H, dd, ^{4}J=1.1Hz, imidazole $C_2\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 29.39 (adamantyl $\underline{C}H$), 35.92 (adamantyl $\underline{C}H_2$), 43.75 (adamantyl $\underline{C}H_2$), 55.01 (adamantyl $\underline{C}_Q$), 115.27 (imidazole $\underline{C}_{4/5}H$), 128.60 (imidazole $\underline{C}_{4/5}H$), 133.52 (imidazole $\underline{C}_2H$) **MS EI**: *m/z* (%) 202 (86, M^+), 135 (100, adamantane) **FTIR (ν_{max} cm^{-1})** KBr 3113 (w), 2920 (s), 2848 (s), 1490 (s), 1230 (s), 930 (s), 813 (s)

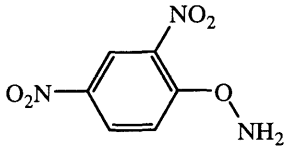
1-(1-Adamantyl)benzimidazole 308[494]



$C_{17}H_{20}N_2$
252.16265 g/mol

The *title compound* was prepared by a literature method.[494] To benzimidazole (3.54 g, 60.0 mmol, 1.82 eq), potassium carbonate (4.14 g, 30.0 mmol, 1.82 eq) and 1,2-dichlorobenzene (10 mL) at 190 °C (graphite bath), 1-bromoadamantane (7.10 g, 33.0 mmol, 1.0 eq) was added portion wise over 1 hour and the temperature of the reaction maintained for a further 4 hours. The hot reaction mixture was filtered and the volatiles were removed *in-vacuo*. The residue was triturated with hexane (5 mL) and the precipitate collected *via* filtration, recrystallised from acetonitrile, and dried *in-vacuo* to give the *title compound* as a cream coloured solid (3.86 g, 15.31 mmol, 46%) **Melting point** 178 – 180 °C, lit.[494] 180 – 184 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.83 (6H, s, adamantyl -C$\underline{H}_2$-), 2.32 (3H, s, adamantyl -C$\underline{H}$-), 2.38 (6H, s, adamantyl -C$\underline{H}_2$-), 7.38 (2H, m, ArC$\underline{H}$), 7.64 (1H, m, ArC$\underline{H}$), 7.86 (1H, m, ArC$\underline{H}$), 8.06 (1H, s, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 29.02 (adamantyl $\underline{C}H$), 35.27 (adamantyl $\underline{C}H_2$), 40.82 (adamantyl $\underline{C}H_2$), 58.14 (adamantyl $\underline{C}_Q$), 114.89 (Ar$\underline{C}H$), 118.11 (Ar$\underline{C}H$), 137.61 (Ar$\underline{C}_Q$), 144.12 (Ar$\underline{C}_Q$), 145.26 (Ar$\underline{C}H$) **MS EI** *m/z* (%): 252 (50, M^+), 135 (80, adamantane), 118 (100, benzimidazole) **FTIR (ν_{max} cm^{-1})** KBr 3405 (br), 3130 (s), 2910 (s), 2850 (s), 2655 (w), 1489 (s), 1224 (s), 1089 (s), 909 (s), 642 (s)

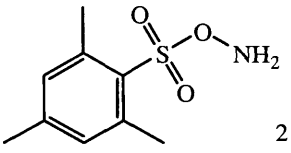
_O_-(2,4-Dinitrophenyl)hydroxylamine 309[519]



$C_6H_5N_3O_5$
199.02292 g/mol

The *title compound* was prepared by a literature method.[519] A solution of hydrazine hydrate (10.0 mL, 0.18 mol, 3.0 eq) in methanol (60 mL) was added in one portion to a solution of 2-(2,4-dinitrophenoxy)-phthalimide **387** (20.0 g, 60.7 mmol, 1.0 eq) in DCM (400 mL) at 0 °C. The reaction mixture rapidly developed a bright yellow colouration, and a precipitate formed. The suspension was allowed to stand at 0 °C for 12 hours, then cold aqueous HCl (400 mL, 1M) was added, and the reaction shaken vigorously at 0 °C. The mixture was filtered through a sintered funnel, and the collected precipitate washed with acetonitrile (50 mL x 3). The filtrate was poured into a separation funnel, and the organic phase separated. The aqueous phase was back extracted with DCM (100 mL x 3) and the combined organic phases were dried over Na_2SO_4, filtered, and the volatiles removed *in-vacuo*. The crude material was recrystallised from ethanol, affording the *title compound* as an orange solid (10.93 g, 54.9 mmol, 90%). **Melting Point** 112 °C, lit.[519] 112 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 6.48 (2H, br s, -N$\underline{H}_2$), 8.08 (1H, d, ^{3}J=9.4Hz, ArC$\underline{H}$), 8.44 (1H, dd, ^{3}J=9.4Hz, ^{4}J=1.7Hz, ArC$\underline{H}$), 8.80 (1H, d, ^{4}J=1.7Hz, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 116.39 (Ar$\underline{C}$H), 121.88 (Ar$\underline{C}$H), 129.35 (Ar$\underline{C}$H), 136.26 (Ar$\underline{C}_Q$), 140.47 (Ar$\underline{C}_Q$), 159.66 (Ar$\underline{C}_Q$) **FTIR** (ν_{max} **cm^{-1}**) film 3331 (w), 3251 (w), 3109 (br), 1588 (s), 1524 (s), 1341 (s), 834 (s), 738 (s)

(2,4,6-trimethylphenyl)sulfonylhydroxylamine 310[495,521]

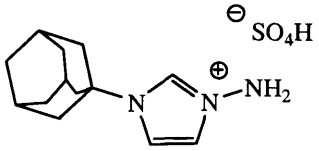


$C_9H_{13}NO_3S$
215.06161 g/mol

The *title compound* was prepared by a literature method.[521] *tert*-Butyl-*N*-(2,4,6-trimethylphenyl)sulphonyloxycarbonate **388** (1.0 g, 3.2 mmol, 1.0 eq) was stirred in

TFA (3.53 mL, 48.0 mmol, 15.0 eq) for 10 minutes at 0°C. The reaction solution was poured onto ice-water (100 mL), and extracted into DCM (30 mL). The volatiles were removed *in-vacuo* and the residue recrystallised from diethyl ether to give the *title compound* as white needles (325 mg, 1.5 mmol, 47%) **Melting point** 93 – 95 °C, lit.[495] 93 – 94 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.15 (3H, s, *p*-ArC$\underline{H}_3$), 2.40 (6H, s, *o*-ArC$\underline{H}_3$), 6.72 (2H, s, ArC$\underline{H}$), 7.11 (2H, br s, N$\underline{H}_2$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 21.09 (*o*-Ar$\underline{C}H_3$), 22.74 (*p*-Ar$\underline{C}H_3$), 114.08 (Ar$\underline{C}_Q SO_2$-), 131.69 (Ar$\underline{C}$H), 140.96 (*p*-Ar$\underline{C}_Q$C H_3), 143.77 (*o*-Ar$\underline{C}_Q CH_3$) **MS (EI):** *m/z* (%) 215 (30, M^+), 199 (50, M^+ -NH_2) **FTIR (ν_{max} cm^{-1})** film 3330 (br, NH), 3260 (s), 1613 (s), 1507 (s), 1251 (s), 1176 (s), 1137 (s), 910 (s), 820 (s)

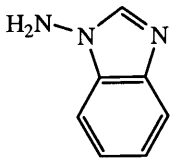
1-Amino-3-Adamantylimidazolium sulphate 311[496]



$C_{13}H_{21}N_3O_4S$
315.12528 g/mol

The *title compound* was synthesised by amination of 1-Adamantyl imidazole **307**, (1.00 g, 4.95 mmol, 1.0 eq) in methanol (40 mL) at 45 °C. Freshly purified hydroxyaminosulphonic acid (0.90 g, 7.90 mmol, 1.6 eq) was dissolved in water (25 mL) and neutralised with $NaHCO_3$ (0.67 g, 7.90 mmol, 1.6 eq) immediately prior to use. The aqueous solution of aminating agent was added to the methanolic solution of **307** over 30 minutes, maintaining the temperature at 45 °C. Stirring the reaction mixture at 45 °C for a further 30 minutes resulted in the formation of a precipitate. The reaction was cooled, and the precipitate isolated *via* filtration. The solid was washed with ice-water gave an amorphous cream/yellow solid (0.28 g, 0.9 mmol, 27%) **Melting Point** 95 – 96 °C, lit.[496] value not quoted **^{1}HNMR** (DMSO-D_6, 300MHz): δ 1.03 (6H, t, ^{3}J=3.1Hz, adamantyl), 1.87 (6H, d, ^{3}J=3.1Hz, adamantyl), 1.47 (3H, br t, ^{3}J=3.1Hz, adamantyl), 6.20 (1H, s, C$\underline{H}$), 6.75 (1H, br s, C$\underline{H}$), 7.26 (1H, br s, C$\underline{H}$) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 29.03 ($\underline{C}$H), 35.43 ($\underline{C}H_2$), 42.96 ($\underline{C}H_2$), 54.57 ($\underline{C}_Q$), 113.70 ($\underline{C}$H), 116.00 ($\underline{C}$H), 127.87 ($\underline{C}$H) MS **ES** *m/z* (%): 337 (40, M^+SO_4Na), 203 (100, M^+SO_4Na-adamantane), 135 (50, adamantane) **FTIR (ν_{max} cm^{-1})** KBr 3420 (NH, br), 3105 (s), 2915 (s), 2855 (s), 1489 (s), 1239 (s), 1099 (SO_4, br), 809 (s)

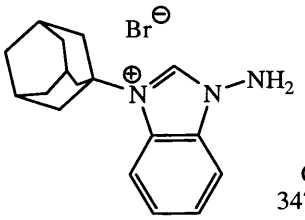
1-aminobenzimidazole 312[497]



$C_7H_7N_3$
133.0640 g/mol

The *title compound* was prepared by a literature method.[497] Freshly purified hydroxylamine-O-sulphonic acid (20.0 g, 0.16 mol, 1.6 eq) was dissolved in water (50 mL) and neutralised using $NaHCO_3$ (13.5 g, 0.16 mol, 1.6 eq). Benzimidazole (11.8 g, 0.1 mol, 1.0 eq) was dissolved in water (80 mL) containing KOH (16.8 g, 0.3 mol, 3.0 eq) and warmed to 40 °C. The neutralised acid was added at a rate to maintain the temperature between 40 – 45 °C, using an ice bath to cool the reaction when necessary. Once the addition was complete, the solution was warmed to between 50 – 55 °C for 30 minutes, during which time a precipitate was formed. The reaction was cooled, the suspension was filtered and the precipitate was washed with cold water to give the *title compound* as white needles (9.5 g, 71.4 mmol, 71%) **Melting Point** 159 °C, lit.[497] 156 – 157 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.36 (2H, s, N$\underline{H}_2$), 7.24 (2H, dddd, ^{3}J=7.3, ^{4}J=1.2Hz, *m*-ArC$\underline{H}$), 7.47 (1H, m, ArC$\underline{H}$), 7.69 (1H, m, ArC$\underline{H}$), 7.92 (1H, s, ArC$\underline{H}$) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 108.73 (Ar$\underline{C}$H), 119.58 (Ar$\underline{C}$H), 121.59 (Ar$\underline{C}$H), 122.43 (Ar$\underline{C}$H), 134.24 (Ar$\underline{C}_Q$), 141.18 (Ar$\underline{C}_Q$), 143.73 (Ar$\underline{C}$H) **MS (EI)** *m/z* (%): 133 (100, M^+), 117 (70, M-NH_2), 106 (85, $C_6H_6N_2$) **FTIR (ν_{max} cm^{-1})** KBr 3305 (s), 3045 (s), 2970 (s), 2109 (w), 1799 (w), 1649 (s), 1499 (s) 1249 (s) 989 (s), 744 (s)

1-amino-3-adamntyl-benzimidazolium bromide 313[498]

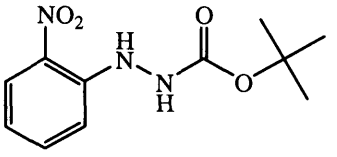


$C_{17}H_{22}BrN_3$
347.09971 g/mol

The *title compound* was prepared by a modified literature method.[498] 1-aminobenzimidazole **312** (7.6 g, 57.1 mmol, 1.0 eq), 1-bromoadamantane (12.3 g, 57.1 mmol, 1.0 eq) and 1,2-dichlorobenzene (1 mL) were combined. The reaction was heated in a graphite bath at 140°C for 2 hours, under atmospheric conditions. The

reaction was cooled to room temperature and the black solid was triturated with acetone to provide a cream solid. The solid was washed with hot acetone to give the *title compound*, as a white solid (1.3 g, 3.6 mmol, 6.3%). **Melting point** >220 °C, lit.[498] 228 – 230 °C (decomp.) **^{1}HNMR** (DMSO-D_6, 300MHz): δ 1.80 (6H, dd, ^{3}J=12.2Hz, adamantyl-C$\underline{H}_2$), 2.27 (3H, s, adamantyl-C$\underline{H}$), 2.37 (6H, s., adamantyl-C$\underline{H}_2$), 6.94 (2H, br s., -N$\underline{H}_2$), 7.63 (1H, dd, ^{3}J=7.6Hz, ArC$\underline{H}$), 7.71(1H, dd, ^{3}J=7.6Hz, ArC$\underline{H}$), 7.97 (1H, dd, ^{3}J=8.2Hz, ArC$\underline{H}$), 8.39 (1H, dd, ^{3}J=8.3Hz, ArC$\underline{H}$), 9.68 (1H, s, benzimidazolium $C_2\underline{H}$) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 29.05 (adamantly-$\underline{C}$H), 34.94 (adamantyl-$\underline{C}H_2$), 40.40 (adamantyl-$\underline{C}H_2$), 61.36 (adamantyl-$\underline{C}_Q$), 113.61 (Ar$\underline{C}$H), 116.62 (Ar$\underline{C}$H), 126.09 (Ar$\underline{C}$H), 126.16 (Ar$\underline{C}$H), 128.05 (Ar$\underline{C}_Q$), 133.06 (Ar$\underline{C}_Q$), 140.47 (benzimidazolium $\underline{C}_2$H) **HRMS (EI)** *m/z* (%): ($C_{17}H_{21}N_3$) Requires 267.17354, Found: 267.17448 (10, M-HBr), 252 (25, M-(HBr+NH_2)), 135 (100, adamantane) **FTIR (ν_{max} cm^{-1})** KBr 3420 (br), 3345 (br), 3295 (br), 3185 (br), 3125 (s), 2920 (s), 2885 (s), 1639 (s), 1539 (s), 1079 (s), 764 (s)

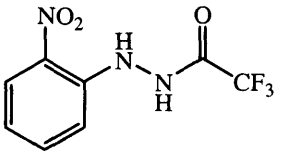
N'-(2-nitro-phenyl)-hydrazinecarboxylic acid *tert*-butyl ester 314[499]



$C_{11}H_{15}N_3O_4$
253.10626 g/mol

The *title compound* was synthesised by addition of Di-*tert*-butyl dicarbonate (713 mg, 3.3 mmol, 1.0 eq) to a solution of 2-Nitrophenyl hydrazine (500 mg, 3.3 mmol, 1.0 eq) in acetonitrile (15 mL). The reaction solution was refluxed for 10 hours, cooled, and the volatiles removed *in-vacuo*. The solid was recrystallised from DCM/petroleum spirit to give the *title compound* as a white solid (645 mg, 25.5 mmol, 78%). **Melting Point** 87 °C lit.[499] 86 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.48 (9H, s, -C(C$\underline{H}_3$)$_3$), 6.58 (1H, s, -N$\underline{H}$-), 6.85 (1H, m, ArC$\underline{H}$), 7.21 (1H, m, ArC$\underline{H}$), 7.51 (1H, m, ArC$\underline{H}$), 8.17 (1H, m, ArC$\underline{H}$) 8.92 (1H, s, -N$\underline{H}$-) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 28.13 (-C($\underline{C}H_3$)$_3$), 82.01 (-$\underline{C}$(CH$_3$)$_3$), 114.14 (Ar$\underline{C}$H), 118.55 (Ar$\underline{C}$H),126.29 (Ar$\underline{C}$H), 132.84 (Ar$\underline{C}_Q$NO$_2$), 136.10 (Ar$\underline{C}$H), 145.70 (Ar$\underline{C}_Q$NH-), 155.15 (-NH$\underline{C}_Q$O-) **MS (EI)** *m/z* (%): 253 (75, M$^+$), 153 (10, M-$C_5H_9O_2$ +H) **FTIR (ν_{max} cm^{-1})** KBr 3465 (br), 3065 (br), 2920 (br), 2555 (br), 1929 (s), 1699 (s), 1669 (s), 1629 (s), 1449 (s), 1339 (br), 1003 (s), 839 (s), 704 (s)

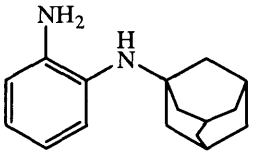
2,2,2-trifluoroacetic acid –*N*'-(2-nitrophenyl)-hydrazide 315



$C_8H_6F_3N_3O_3$
249.03613 g/mol

The *title compound* was synthesised by the addition of trifluoroacetic anhydride (0.53 mL, 3.8 mmol, 1.2 eq) to a solution of 2-Nitrophenyl hydrazine (500 mg, 3.3 mmol, 1.0 eq) in THF (15 mL) at 0 °C. The reaction solution was stirred at room temperature for 30 hours during which time a red colouration developed. The volatiles were removed *in-vacuo* and the crude material washed with petroleum spirit (10 mL x 2), and dried *in-vacuo* to give the *title compound* as a yellow powder (560 mg, 2.3 mmol, 70%). **Melting Point** 160 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 6.95 (1H, dd, ^{3}J=7.5Hz, ^{4}J=0.4Hz, ArC*H*), 7.04 (1H, d, ^{3}J=8.6Hz, ArC*H*), 7.64 (1H, dd, ^{3}J=7.5Hz, ^{4}J=0.4Hz, ArC*H*), 8.14 (1H, d, ^{3}J=8.6Hz, ArC*H*) 9.54 (1H, s, -N*H*-), 11.80 (1H, br s, -N*H*-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 114.17 (Ar*C*H), 115.14 (d, ^{1}J=288.2Hz, CF_3), 118.68 (Ar*C*H), 126.03 (Ar*C*H), 132.29 (ArC_Q), 136.65 (Ar*C*H), 143.51 (ArC_Q), 156.37 (d, ^{2}J=35.80Hz *C*=O) **^{19}FNMR** (DMSO-D_6, 282.2MHz): δ -74.10 (-C*F*$_3$) **HRMS (CI)** methane *m/z* (%): ($C_8H_6F_3N_3O_3$) Requires 250.04395, Found: 250.04369 (100) M^+, 232 (75) $C_8H_6F_3N_3O_2$, 137 (90) $C_6H_5N_2O_2$ **FTIR (ν_{max} cm^{-1})** KBr 3370 (NH, s), 3300 (NH, br), 3105 (w), 1749 (s), 1619 (CO, s), 1489 (s), 1269 (s), 1159 (br), 744 (s)

1-(1-adamantylamino)-2-aminobenzene 318

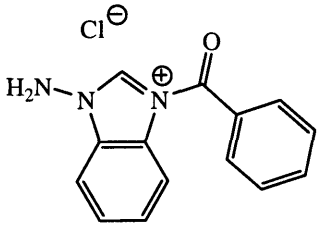


$C_{16}H_{22}N_2$
242.1783 g/mol

The *title compound* was synthesised by addition of 1,2-diaminobezene (5.00 g, 46.2 mmol, 1.0 eq), 1-bromoadamantane (9.95 g, 46.2 mmol, 1.0 eq), K_2CO_3 (6.32 g, 46.2 mmol, 1.0 eq), and 1,2-dichlorobenzene (1 mL) to a round-bottomed flask that was heated to 150°C for 2 hours in a graphite bath. The reaction was cooled, and extracted with $CHCl_3$ (75 mL x 2). The organic layer was filtered, and the volatiles were removed *in-vacuo*. The solid was washed with ether (50 mL x 2) to give the *title*

compound as a yellow powder (5.53 g, 22.8 mmol, 50%). **Melting Point** 123 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.59 (6H, s, adamantyl-C$\underline{H}_2$), 2.06 (3H, s., adamantyl-C$\underline{H}$), 2.15 (6H, d, ^{3}J=2.4Hz, adamantyl-C$\underline{H}_2$), 6.72 (2H, m, ArC$\underline{H}$), 7.13 (1H, ddd, ^{3}J=7.4Hz, ^{4}J=1.3Hz, ArC$\underline{H}$), 7.55 (1H, dd, ^{3}J=7.90Hz, ^{4}J=1.2Hz, ArC$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 29.36 (adamantly-$\underline{C}$H), 35.25 (adamantyl-$\underline{C}H_2$), 38.88 (adamantyl-$\underline{C}H_2$), 65.80 (adamantyl-C_Q), 115.93 (Ar$\underline{C}_Q$), 117.95 (Ar$\underline{C}$H), 118.64 (Ar$\underline{C}$H), 128.19 (Ar$\underline{C}$H), 130.24 (Ar$\underline{C}$H), 142.46 (Ar$\underline{C}_Q$) **HRMS (Positive Ion FAB)** *m/z* (%): ($C_{16}H_{22}N_2$+H) Requires 243.18612, Found: 243.18632 (85, M^+H), 352 (25, $C_6H_9N_2$) **FTIR (ν_{max} cm^{-1})** KBr 3350 (NH, br), 3250 (NH, s), 3215 (NH, s), 2910 (br), 2750 (br), 2495 (br), 1649 (s), 1509 (s), 1052 (s), 795 (s)

1-amino-3-phenacetyl-benzimidazolium chloride 320

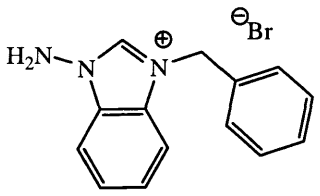


$C_{14}H_{12}ClN_3O$
273.06689 g/mol

The *title compound* was synthesised by the addition of benzoyl chloride (0.89 mL, 7.5 mmol, 1.0 eq) to a refluxing solution of 1-aminobenzimidazole **312** (1.0 g, 7.5 mmol, 1.0 eq) in acetonitrile (15 mL). The reaction was maintained at reflux for 1 hour, before it was cooled to room temperature and the precipitate collected *via* filtration. A second crop of material was available by addition of ether to the mother liquor, which led to further precipitation of product. The combined solids were washed with ether, then petrol, followed by removal of volatiles *in-vacuo* to give the *title compound* as a white powder (1.3 g, 5.3 mmol, 71%) **Melting Point** >220 °C **^{1}HNMR** (MeOD, 300MHz): δ 7.80 (2H, m, ArC$\underline{H}$), 7.90 (3H, m, ArC$\underline{H}$), 7.99 (1H, m, ArC$\underline{H}$), 8.13 (1H, m, ArC$\underline{H}$), 8.19 (1H, m, ArC$\underline{H}$), 8.32 (1H, m, ArC$\underline{H}$), 10.05 (1H, s, N=C$\underline{H}$N) **^{13}CNMR** (MeOD, 75.5MHz): δ 113.06 (Ar$\underline{C}$H), 115.47 (Ar$\underline{C}$H), 116.40 (Ar$\underline{C}$H), 128.74 (Ar$\underline{C}$H), 128.83 (Ar$\underline{C}$H), 129.28 (Ar$\underline{C}$H), 130.13 (Ar$\underline{C}$H), 131.06 (Ar$\underline{C}_Q$), 131.37 (Ar$\underline{C}_Q$), 132.55 (Ar$\underline{C}_Q$), 134.76 (Ar$\underline{C}$H), 168.35 (Ar$\underline{C}_Q$O) **HRMS (Positive Ion FAB)** *m/z* (%): ($C_{14}H_{12}ClN_3O$ +H-Cl) Requires 238.09749, Found: 238.09758 (100, M^+H-Cl), 154 (60)

FTIR (ν_{max} cm^{-1}) KBr 3480 (br), 3099 (br), 2988 (br), 2801 (br), 1893 (w), 1698 (CO, s), 1654 (s), 1525 (s), 1481 (s), 1442 (s), 1261 (s), 824 (s), 749 (s)

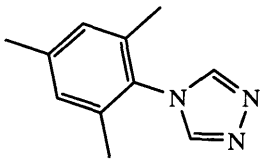
1-amino-3-benzyl-benzimidazolium bromide 321[500]



$C_{14}H_{14}BrN_3$
303.03711 g/mol

The *title compound* was synthesised by addition of a solution of benzyl bromide (0.89 mL, 7.5 mmol, 1.0 eq) in acetonitrile (2 mL) to a refluxing solution of 1-aminobenzimidazole **312** (1.0 g, 7.5 mmol, 1.0 eq) in acetonitrile (5 mL). The reaction solution was refluxed for 12 hours during which time the product precipitated. The precipitate was collected *via* filtration, washed with ether and dried *in-vacuo* to give the *title compound* as a white solid (1.9 g, 6.3 mmol, 84%). **Melting Point** 141 – 143 °C, lit.[500] 145 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.81 (2H, s, -C$\underline{H}_2$), 7.33 (4H, m, ArC$\underline{H}$), 7.53 (2H, d, ^{3}J=7.1Hz, ArC$\underline{H}$), 7.63 (2H, quin, ^{3}J=7.5Hz, ArC$\underline{H}$), 7.96 (2H, d, ^{3}J=8.3Hz, ArC$\underline{H}$), 10.15 (1H, d, ^{3}J=2.7Hz, N=C$\underline{H}$N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 49.67 ($\underline{C}H_2$), 113.20 (Ar$\underline{C}$H), 115.14 (Ar$\underline{C}$H), 126.91 (Ar$\underline{C}$H), 129.26 (Ar$\underline{C}$H), 129.67 (Ar$\underline{C}$H), 130.32 (Ar$\underline{C}_Q$), 131.75 (Ar$\underline{C}_Q$), 132.52 (Ar$\underline{C}$H), 133.27 (Ar$\underline{C}_Q$), 133.51 (Ar$\underline{C}$H), 135.95 (Ar$\underline{C}$H), 142.76 (Ar$\underline{C}$H) **HRMS (FAB)** *m/z* (%): ($C_{14}H_{14}BrN_3$ +H-Br) Requires 225.12659, Found: 225.12715 (100, M^+H-Br), 192 (10) **FTIR (ν_{max} cm^{-1})** KBr 3435 (NH, br), 3220 (s), 3110 (s), 3000 (s), 1804 (w), 1614 (s), 1554 (s), 1459 (s), 1194 (s), 989 (w), 755 (s)

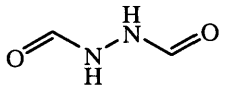
4-Mesityl-1,2,4-triazole 324[501, 502]



$C_{11}H_{13}N_3$
187.11095 g/mol

The *title compound* was prepared according to a modified a literature method.[501] *N-N'*-diformylhydrazine **325** (0.75 g, 8.50 mmol, 1.0 eq) was heated with mesityl aniline (1.44 mL, 10.22 mmol, 1.2 eq) in the presence of $(NH_4)_2SO_3$ (110 mg, 0.85 mmol, 0.1 eq) at 180 °C in a graphite bath for 3 hours. The reaction was cooled to room temperature and the residue was recrystallised from toluene and washed with ether. A further recrystallisation from ethanol gave the *title compound* as a white plates (610 mg, 3.39 mmol, 39%) **Melting Point** >220 °C, lit.[502] 232 – 233 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 2.09 (6H, s, *o*-C$\underline{H}_3$), 2.21 (3H, s, *p*-C$\underline{H}_3$), 6.87 (2H, s, ArC$\underline{H}$), 8.21 (2H, m, =NC$\underline{H}$N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 18.20 (*o*-C$\underline{H}_3$), 20.48 (*p*-C$\underline{H}_3$), 128.28 (Ar$\underline{C}$H), 131.36 (Ar$\underline{C}_Q$), 134.40 (Ar$\underline{C}_Q$), 135.52 (Ar$\underline{C}_Q$), 159.40 (=NC$\underline{H}$N) **HRMS (EI)** *m/z* (%): ($C_{11}H_{13}N_3$ +H) Requires 188.11877, Found: 187.11891 (80, M^+H) **FTIR (ν_{max} cm^{-1})** KBr 3210 (br), 3000 (s), 2920 (s), 2865 (s), 2770 (w), 1664 (s), 1529 (s), 1259 (s), 1024 (w), 854 (s)

N-N'-Diformylhydrazine 325[503]

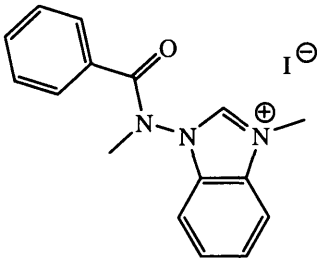


$C_2H_4N_2O_2$
88.02728 g/mol

The *title compound* was prepared according to a modified literature method.[503] Hydrazine hydrate (2.5 mL, 50.0 mmol, 1.0 eq) and formamide (4.5 g, 0.1 mol, 2.0 eq) were heated to 100 °C for 4 hours in the absence of solvent. The volatiles were removed *via* distillation *in-vacuo* and ethanol (5 mL, 96%) added to the residue in order to triturate the *title compound* as a white solid (1.8 g, 19.9 mmol, 40%). **Melting point** 158 °C, lit.[503] 159 – 160 °C **^{1}HNMR** (D_2O, 300MHz): δ 8.16 (2H, s, $\underline{H}$CON-) **^{13}CNMR** (D_2O, 75.5MHz): δ 158.83 (H$\underline{C}$ON-) **HRMS (EI)** *m/z* (%): ($C_2H_4N_2O_2$) Requires

88.02728, Found: 88.02719 (70, M^+), 60 (100, M^+-CHO) **FTIR (ν_{max} cm^{-1})** KBr 3550 (br, NH), 3190 (br), 1696 (br, CO), 1604 (br), 1479 (br), 1399 (s), 1219 (w), 764 (br)

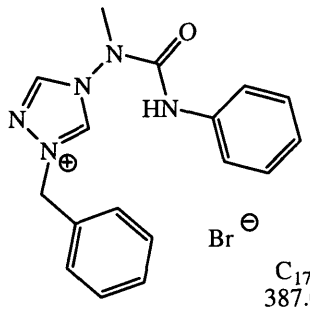
1-(*N*-phenacetyl-*N*-methylamino)-3-methyl-benzimidazolium iodide 327[504]



$C_{16}H_{16}IN_3O$
393.03381 g/mol

The *title compound* was prepared according to modification of a literature method.[504] **281** (250.0 mg, 0.66 mmol, 1.0 eq), K_2CO_3 (214.0 mg, 1.32 mmol, 2.0 eq) and MeI (3.0 mL, 37.20 mmol, 56.4 eq) were added to acetone (3 mL). The reaction was stirred for 1 week at room temperature, filtered and the volatiles removed *in-vacuo*. Recrystallisation of the residue from ethanol, gave the *title compound* as a white solid that was dried *in-vacuo* (136 mg, 0.34 mmol, 52%) **Melting Point** 195 °C, lit.[504] 194 – 195 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 3.62 (-C$\underline{H}_3$), 4.16 (-C$\underline{H}_3$), 7.51 (3H, m, ArC$\underline{H}$), 7.75 (4H, m, ArC$\underline{H}$), 8.11 (1H, m, ArC$\underline{H}$), 8.17 (1H, m, ArC$\underline{H}$), 10.42 (1H, s, N=C$\underline{H}$N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 34.06 ($\underline{C}H_3$), 39.51 ($\underline{C}H_3$), 112.47 (Ar$\underline{C}$H), 113.61 (Ar$\underline{C}$H), 114.30 (Ar$\underline{C}$H), 127.27 (Ar$\underline{C}$H), 127.73 (Ar$\underline{C}$H), 127.84 (Ar$\underline{C}$H), 128.60 (Ar$\underline{C}$H), 129.45 (Ar$\underline{C}_Q$), 130.24 (Ar$\underline{C}_Q$), 131.68 (Ar$\underline{C}_Q$), 131.84 (Ar$\underline{C}$H), 169.84 (Ar$\underline{C}_Q$) **MS (EI)** *m/z* (%): 142 (35), 134 (25), 105 (90), **FTIR (ν_{max} cm^{-1})** KBr 3111 (s), 3020 (br), 2845 (w), 1646 (CO, s), 1575 (s), 1549 (s), 1470 (s), 1267 (s), 891 (s)

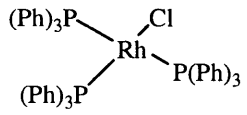
1-phenyl-3-(*N*-methyl-*N*-(1-benzyl-1,2,4-triazolium))-urea bromide 328



$C_{17}H_{18}BrN_5O$
387.06947 g/mol

The *title compound* was synthesised by refluxing a suspension of **283** (1.0 g, 2.7 mmol, 1.0 eq) in acetonitrile (30 mL, reagent grade) until complete dissolution was observed. MeI (32.2 mL, 26.8 mmol, 10.0 eq) was added over 3 hours, and the reaction maintained at reflux for a further 2 hours, during which time a white precipitate formed. The hot reaction solution was filtered, the collected precipitate washed with ether and dried *in-vacuo* to give the *title compound* as a white powder (0.63 g, 1.6 mmol, 61%) **Melting Point** 210 °C (decomp.) **^{1}HNMR** (DMSO-D_6, 300MHz): δ 3.62 (3H, m, CH_3), 5.71 (2H, s, CH_2), 7.10 (1H, m, ArC*H*), 7.34 (2H, m, ArC*H*), 7.48 (7H, m, ArC*H*), 9.46 (1H, s, N*H*), 9.71 (1H, s, N=C*H*N), 10.78 (1H, m, $^+$N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 40.65 (*C*H_3) 55.58 (*C*H_2) 120.82 Ar*C*H), 123.99 (Ar*C*H), 128.69 (Ar*C*H), 129.12 (Ar*C*H), 129.22 (multiple Ar*C*H), 132.41 (Ar*C*$_Q$), 137.99 (Ar*C*$_Q$) 153.95 (Ar*C*$_Q$O) **HRMS (CI)** methane *m/z* (%): ($C_{17}H_{18}BrN_5O$ +H-Br) Requires 309.15895, Found: 309.16004 (40, M^+H-Br), 120 (30, C_7H_6NO) **FTIR (ν_{max} cm^{-1})** KBr 3255 (br, =NH), 2960 (br), 1689 (s) (CO), 1524 (s), 1314 (s), 1234 (s)

Wilkinson's Catalyst 334[461, 505]

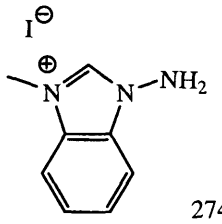


$C_{54}H_{45}ClP_3Rh$
924.14777 g/mol

The *title compound* was prepared by a literature method.[505] $RhCl_3.3H_2O$ (2.00 g, 7.64 mmol, 1.0 eq) was dissolved in ethanol (70 mL, 96%) and a solution of triphenyl phosphine (12.00 g, 45.80 mmol, 6.0 eq) in hot ethanol (250 mL) was added under N_2. Anti-bumping granules were added to the reaction mixture, which was heated to reflux

for 3 hours using a heating mantle. During the reaction a burgundy red crystalline material precipitated, which was collected *via* filtration of the hot reaction. The collected solid was washed with ether (3 x 20 mL), and dried *in-vacuo* to give the *title compound* as a burgundy crystalline powder (5.86 g, 6.34 mmol, 83%) **Melting point** 133 - 134 °C, lit.[461] 132 – 134 °C **^{1}HNMR** (CD_2Cl_2, 500MHz): δ 6.89 – 7.21 (10H, m, ArC*H*), 7.41 – 7.65 (30H, m, ArC*H*) 13CNMR (CD_2Cl_2, 125.75MHz): δ128.89 (Ar*C*H), 129.05 (Ar*C*H), 129.09 (br, Ar*C*H), 132.32 (Ar*C*$_Q$), 132.34 (br, Ar*C*H), 132.47 (Ar*C*H) 31PNMR (CD_2Cl_2, 202.50MHz): δ 32.59 (PPh_3 trans to $RhPPh_3$), 48.53 (PPh_3 trans to RhCl)

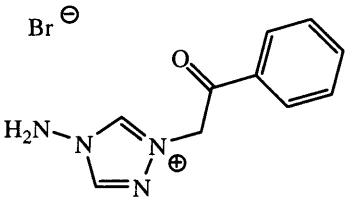
1-amino-3-methylbenzimidazolium iodide 340[506]



$C_8H_{10}IN_3$
274.99194 g/mol

The *title compound* was synthesised by the addition of MeI (0.83 mL, 13.5 mmol, 1.5 eq) *via* syringe pump over 1 hour to a refluxing solution of 1-aminobenzimidazole **312**, (1.2 g, 9.0 mmol, 1.0 eq) in ethanol (5 mL, 99.6%). The reaction was stirred at reflux for 3 hours, cooled and the precipitate collected *via* filtration. The crude material was washed with ethanol, and ether before being dried *in vacuo* to give the *title compound* as a white solid (2.3 g, 8.4 mmol, 93%). **Melting Point** 212 °C, lit.[506] 205 – 207 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 4.09 (3H, s, -C*H*$_3$), 6.93 (2H, s, -N*H*$_2$), 7.66 (2H, m, ArC*H*), 7.92 (2H, m, ArC*H*), 9.76 (1H, s, N=C*H*N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 33.25 (*C*H_3), 112.92 (Ar*C*H), 113.13 (Ar*C*H), 126.17 (Ar*C*H), 126.34 (Ar*C*H), 130.37 (Ar*C*$_Q$), 131.76 (Ar*C*$_Q$), 142.30 (Ar*C*H) **HRMS (EI)** *m/z* (%) ($C_8H_{10}IN_3$ -I) Requires 148.08747, Found: 148.08843 (10, M^+-I), 254 (50), 132 (100, M^+-I-NH_2), 105 (25, benzimidazole) **FTIR (ν_{max} cm^{-1}) KBr** 3460 (br) 3235 (s), 3095 (w), 3050 (s), 3015 (s), 1629 (s), 1604 (s), 1264 (s), 759 (s), 749 (s)

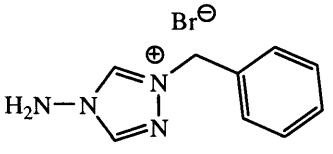
1-amino-3-phenacyl-1,2,4-triazolium bromide 341



$C_{10}H_{11}BrN_4O$
282.01162 g/mol

The *title compound* was synthesised by dropwise addition of 2-bromoacetophenone (4.72 g, 23.8 mmol, 1.0 eq) as a solution in acetonitrile (12 mL) to a solution of 4-amino-1,2,4-triazole **381** (2.00 g, 23.8 mmol, 1.0 eq) in refluxing acetonitrile (12 mL), which resulted in precipitation of a white solid. The reaction was stirred at reflux for a further 5 minutes, cooled, filtered, and the collected solid washed with ether, then petroleum spirit, after which the volatiles were removed *in-vacuo* to yield the *title compound* as a white powder (6.20 g, 22.0 mmol, 93%) **Melting Point** 178 – 179 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 6.88 (2H, s, CH_2), 7.30 (2H, br s, N$\underline{H}_2$), 7.63 (2H, t, ^{3}J=7.5Hz, *m*-ArC$\underline{H}$), 7.77 (1H, t, ^{3}J=7.5Hz, *p*-ArC$\underline{H}$), 8.08 (2H, ^{3}J=7.5Hz, *o*-ArC$\underline{H}$), 9.87 (1H, s, -N-C$\underline{H}$=N-), 10.31 (1H, d, ^{4}J=4.4Hz, -N-C$\underline{H}$=N$^+$-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 58.58 (-$\underline{C}H_2$-), 128.39 (Ar$\underline{C}$H), 129.14 (Ar$\underline{C}$H), 133.38 (Ar$\underline{C}_Q$), 134.78 (Ar$\underline{C}$H), 143.97 (N-$\underline{C}$H=N$^+$), 145.15 (N-$\underline{C}$H=N$^+$), 190.55 ($\underline{C}_Q$O) **HRMS (ES)** *m/z* (%): ($C_{10}H_{11}BrN_4O$ -Br) Requires 203.09274, Found: 203.09251 (85, M$^+$-Br) **FTIR (ν_{max} cm^{-1})** KBr 3150 (s), 3125 (s), 3035 (br), 2915 (s), 1689 (CO, s), 1364 (s), 1239 (s), 764 (s), 619 (s)

1-amino-3-benzyl-1,2,4-triazolium bromide 342[507]

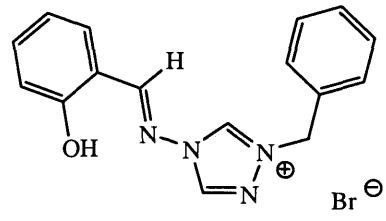


$C_9H_{11}BrN_4$
254.01671 g/mol

The *title compound* was prepared according to modification of a literature method.[507] Benzyl bromide (2.83 mL, 23.8 mmol, 1.0 eq) was added dropwise as a solution in acetonitrile (12 mL) to a solution of 4-amino-1,2,4-triazole **381** (2.00 g, 23.8 mmol, 1.0 eq) in refluxing acetonitrile (12 mL) and K_2CO_3 (3.28 g, 23.8 mmol, 1.0 eq). The

reaction solution was maintained at reflux for a further 5 hours, filtered whilst hot and cooled to room temperature. The product precipitated as a white solid, which was collected *via* filtration, washed with ether, then petroleum spirit and the volatiles removed in-*vacuo* to give the *title compound* as a white powder (5.21 g, 20.5 mmol, 86%) **Melting Point** 139 °C, lit.[507] 141 – 143 °C (ethanol) **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.58 (2H, s, -C*H*$_2$-), 7.38 (5H, m, ArC*H*), 9.91 (1H, br s, N=C*H*-N), 10.97 (1H, br s, -N-C*H*=N$^+$-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 55.31 (-*C*H$_2$-), 123.16 (Ar*C*H), 124.15 (Ar*C*H), 128.25 (Ar*C*H), 128.79 (Ar*C*H), 129.30 (Ar*C*H), 134.01 (Ar*C*$_Q$), 140.16 (-N=*C*H-), 164.83 (N-*C*H=N$^+$) **MS (EI)** *m/z* (%): 175.10 (90, M), 91 (65, C_7H_7), 84 (40), 77 (55) **FTIR (ν_{max} cm^{-1}) KBr** 3475 (br, NH), 3335 (m), 3004 (s), 1620 (s), 1535 (s), 1471 (s), 1055 (s), 714 (s)

4-[(2-Hydroxy-benzylidine)-amino]-1-benzyl-(1,2,4-triazolium) bromide 343

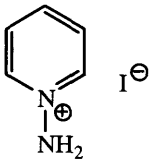


$C_{16}H_{15}BrN_4O$
358.04292 g/mol

The *title compound* was synthesised by the addition of benzyl bromide (314 μl, 2.7 mmol, 1.0 eq) diluted in acetonitrile (2 mL), to a refluxing suspension of 2-((4*H*-1,2,4-triazol-4-ylimino)methyl)phenol **385** (500 mg, 2.7 mmol, 1.0 eq) in acetonitrile (10 mL). After the addition, the reaction became homogeneous and developed a yellow colour. The solution was maintained at reflux for 4 hours, before being cooled to room temperature. The *title compound* precipitated from the reaction solution and was collected *via* filtration, washed with ether, then petroleum spirit to give the *title compound* as a cream coloured solid (667 mg, 1.8 mmol, 63%) **Melting Point** 208 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 5.69 (2H, s, -C*H*$_2$-), 6.98 (1H, t, ^{3}J=7.5Hz, ArC*H*), 7.09 (2H, dd, ^{3}J=7.9Hz, ^{4}J=0.5Hz, ArC*H*), 7.43 (3H, m, ArC*H*), 7.52 (3H, dd, ^{3}J=7.7Hz, ^{4}J=1.8Hz, ArC*H*), 7.86 (1H, d, ^{3}J=7.4Hz, ArC*H*), 9.83 (1H, s, -N-C*H*=N-), 9.88 (1H, s, -N=C*H*-), 10.81 (1H, s, -N-C*H*=N$^+$-), 11.06 (1H, br s, O*H*) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 55.16 (-*C*H$_2$-), 113.69 (Ar*C*H), 116.99 (Ar*C*H), 119.86 (Ar*C*H), 127.35 (Ar*C*H), 128.82 (Ar*C*H), 128.92 (Ar*C*$_Q$CH$_2$-), 128.96 (Ar*C*H), 133.08 (Ar*C*$_Q$), 135.71 (Ar*C*H), 139.40 (Ar*C*H), 140.58 (-N=*C*H-), 159.29 (Ar*C*$_Q$CH=N-), 161.15 (-N*C*H=N$^+$-)

HRMS (FAB) *m/z* (%): ($C_{16}H_{15}BrN_4O$ +H-Br) Requires 280.13240, Found: 280.13178 (100, M^+H), 187 (25, $C_9H_7N_4O$) **FTIR** (ν_{max} **cm^{-1}**) KBr 3440 (w, =NH), 3115 (br, OH), 3010 (s), 1609 (s), 1569 (s), 1454 (s), 1049 (s), 714(s) **Elemental analysis** Calculated C 53.50%, H 4.21%, N 15.60%; Found C 52.39%, H 4.20%, N 15.18%

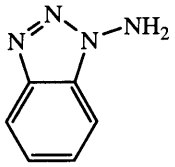
1-Aminopyridinium Iodide 349[508, 509]



$C_5H_7IN_2$
221.96539 g/mol

The *title compound* was prepared by a literature method.[508] Freshly purified hydroxylamine-O-sulphonic acid (5.65 g, 50.0 mmol, 1.0 eq) was dissolved in cold water (0 °C, 32 mL), and freshly distilled pyridine (12 mL, 0.15 mol, 3.0 eq) was added. The mixture was heated to 90 °C for 30 minutes, cooled to room temperature and K_2CO_3 (6.90 g, 50.0 mmol, 1.0 eq) added. The volatiles were removed *in-vacuo* and the residue extracted with ethanol (60 mL, 99.6%), and filtered. The filtrate was cooled to -25 °C and HI (7 mL, 50.0 mmol, 1.0 eq) added. The solution was aged for 1 hour at –25 °C, before being filtered. Recrystallisation of the crude solid from ethanol (50 mL) gave the *title compound* as a cream coloured powder (6.81 g, 30.7 mmol, 61%) **Melting Point** 164 – 165 °C, lit.[509] 161 – 162 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 7.09 (2H, dd, ^{3}J=7.3 ArC*H*), 8.25 (1H, dddd, ^{3}J=7.8Hz, ^{4}J=0.9Hz, *p*-ArC*H*), 8.40 (2H, s, NH_2), 8.73 (2H, dd, ^{3}J=7.0Hz, ^{4}J=0.7Hz, *o*-ArC*H*) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 112.44 (*m*-ArCH), 138.31 (*o*-ArCH), 139.85 (*p*-ArCH) **MS (EI)** *M/z* (%): 95 (100, M-I), (100, $C_5H_7N_2^+$) **FTIR** (ν_{max} **cm^{-1}**) **KBr** 3468 (br), 3180 (br), 3064 (s), 1507 (s), 1477 (s), 905 (br), 794 (s), 759 (s)

1-aminobenzatriazole 371[510, 511]



$C_6H_6N_4$
134.05925 g/mol

The *title compound* was prepared by a literature method.[510] Freshly purified hydroxylamine-*O*-sulphonic acid (31.68 g, 0.28 mol, 2.0 eq) was added portion wise to a stirred solution of benzatriazole (16.68 g, 0.14 mol, 1.0 eq) and potassium hydroxide (39.30 g, 0.7 mol) in water (170 mL), maintaining the temperature of the reaction mixture below 40 °C by use of an ice bath. After the addition was complete, the mixture was cooled to room temperature and stirred for a further 2.5 hours. The precipitate that formed was removed *via* vacuum filtration and washed thoroughly with ether. The organic phase was separated and the aqueous layer extracted with ether (5 x 100 mL). The combined ether solutions were dried and the volatiles were removed *in-vacuo*. The crude product was dissolved in a minimum of hydrochloric acid (50 mL, 2M) and the resulting solution kept at -10 °C overnight during which time 1-aminobenzotriazole hydrochloride precipitated and was isolated *via* filtration. The free amine was obtained by direct basification of the salt using aqueous sodium hydroxide (50 mL, 2M) followed by extraction with ether (3 x 100 mL). The combined extracts were dried and the volatiles were removed *in-vacuo* to give the *title compound* as a white solid (5.31 g, 39.3 mmol, 28%) **Melting point** 79 – 81 °C, lit.[511] 84 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 5.77 (2H, s, N*H*$_2$), 7.31 (1H, dddd, ^{3}J=7.9Hz, ^{4}J=0.9Hz, ArC*H*), 7.45 (1H, dddd, ^{3}J=7.9Hz, ^{4}J=0.9Hz, ArC*H*), 7.59 (1H, ddd, ^{3}J=8.4Hz, ^{4}J=0.9Hz, ArC*H*), 7.93 (1H, ddd, ^{3}J=8.4Hz, ^{4}J=0.9Hz, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 109.78 (Ar*C*H), 119.66 (Ar*C*H), 124.05 (Ar*C*H), 127.70 (Ar*C*H), 132.41 (Ar*C*$_Q$), 144.44 (Ar*C*$_Q$) MS **(ES)** *m/z* (%): 133 (15, M-H), 120 (100, M-NH_2^+H) **FTIR (ν_{max} cm^{-1}) KBr** 3332 (NH, s), 3226 (NH, br), 3125 (br), 3008 (br), 1957 (w), 1643 (s), 1411 (s), 1274 (s), 1239 (s), 1047 (br), 744 (s)

Hydroacylation

The following the general method was used to investigate the activity of our novel ligand range for the rhodium catalysed hydroacylation of alkenes. Chapter 7 of this thesis discusses its development and demonstrates its effectiveness.

Hydroacylation method A

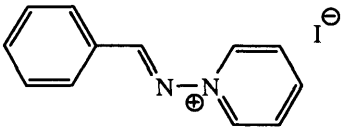
Freshly distilled benzaldehyde (1.0 mmol), ligand (0.2 eq), TFA (0.1 eq) and 1-hexene (5.0 eq) were combined in an ampoule and toluene (1 mL) added. The solution was stirred at room temperature for 15 minutes and $RhCl(PPh_3)_3$ **334** (2 mol%) added. The ampoule was sealed and the reaction heated to 130 °C for 12 hours. The reaction was cooled to room temperature and the dark solution purified by column chromatography.

The following compounds from hydroacylation reactions were analysed by ^{1}HNMR, ^{13}CNMR and where appropriate, melting point and were found to have identical spectral and physical properties to authentic samples.

***N*-Benzylideneaniline 373**

Heptaphenone 375

1-Benzylidenimine-pyridinium Iodide 376[512]

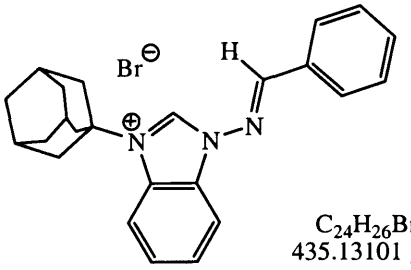


$C_{12}H_{11}IN_2$
309.99669 g/mol

The *title compound* was synthesised by the addition of benzaldehyde (276μl, 0.45 mmol, 1.0 eq) to a solution of *N*-aminopyridinium iodide **349** (100 mg, 0.45 mmol, 1.0 eq) in ethanol (5 mL). The reaction solution was heated to reflux for 5 hours, cooled to room temperature and layered with *n*-hexane (3 mL) that precipitated the product. The yellow precipitate was collected *via* filtration and dried *in vacuo* to give the *title compound* as yellow needles (121 mg, 0.39 mmol, 87%) **Melting Point** 160 – 161 °C (decomp.), lit.[512] 161.5 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 7.67 (2H, dddd, ^{3}J=7.8Hz

ArC*H*), 7.76 (1H, ddd, ^{3}J=7.1Hz, ^{4}J=1.1Hz, ArC*H*), 8.02 (2H, dd, ^{3}J=7.2Hz, ^{4}J=1.6Hz, ArC*H*), 8.31 (2H, dd, ^{3}J=7.2Hz, ^{4}J=1.6Hz, ArC*H*), 8.69 (1H, dddd, ^{3}J=7.7Hz, ^{4}J=2.3Hz, ArC*H*), 9.81 (1H, d, ^{4}J=2.7Hz, -N=C*H*-), 9.88 (2H, dd, ^{3}J=6.0, ^{4}J=0.8Hz ArC*H*) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 113.61 (*m*-PyridineCH), 128.41 (*p*-BenzylCH), 129.49 (*m*-BenzylCH), 130.16 (*o*-BenzylCH), 130.38 (BenzylC_Q), 134.43 (*o*-PyridineCH) 139.84 (ArCH), 145.14 (*o*-PyridineCH), 170.30 (imine CH) **HRMS ES** *m/z* (%): ($C_{12}H_{11}IN_2$) Requires 183.09167, Found: 183.09161 (100, M^+), 493 (20, [M-I-M]$^+$) **FTIR (ν_{max} cm^{-1})** KBr 3440 (=NH, br) 3100 (s), 3025 (br) 1624 (s), 1564 (s), 1474 (s), 1379 (s), 979 (s), 764 (s)

1-benzylideneamino-3-adamantyl-benzimidazolium bromide 378



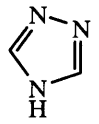
$C_{24}H_{26}BrN_3$
435.13101 g/mol

The *title compound* was synthesised by addition of benzaldehyde (425 µl, 3.8 mmol, 1.2 eq) to a refluxing solution of **313** (1.10 g, 3.2 mmol, 1.0 eq) in ethanol (20ml, 99.6%). The salt occasionally required several minutes at reflux before complete dissolution was observed. The reaction was maintained at reflux for 3 hours, during which time a white precipitate formed. The volatiles were removed *in-vacuo* and the white solid washed with ether to give the *title compound* as a white powder (1.38 g, 3.2 mmol, 100%) **Melting point** >220 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.91 (6H, br s., adamantyl-CH_2), 2.47 (3H, s, adamantyl-CH), 2.66 (6H, d, ^{3}J=2.1Hz, adamantyl-CH_2), 7.54 (3H, m, ArCH), 7.69 (2H, m, ArCH), 8.09 (2H, m, benzimidazolium ArCH), 8.29 (2H, m, ArCH), 10.76 (1H, s, N=CH), 11.32 (1H, s, benzimidazolium C_2H) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 29.55 (adamantly-CH), 35.47 (adamantyl-CH_2), 42.05 (adamantyl-CH_2), 64.36 (adamantyl-C_Q), 114.39 (ArCH), 116.07 (ArCH), 126.78 (ArCH), 127.10 (ArCH), 128.45 (ArC_QN), 128.49 (ArCH), 130.06 (ArCH), 131.49 (ArC_QN), 131.83 (ArC_QC=N), 133.10 (ArCH), 133.45 (benzimidazolium C_2H) 163.66 (N=CH) **HRMS (ES)** *m/z* (%): ($C_{24}H_{26}BrN_3$ –Br) Requires 356.21212, Found:

356.21248 (100, M^+-Br) **FTIR (ν_{max} cm^{-1})** KBr 3420 (=NH, br), 3075 (s), 3020 (s), 2975 (s), 2910 (s), 2890 (s), 2855 (s), 1619 (w), 1519 (s), 1224 (s), 754 (s)

Intermediates

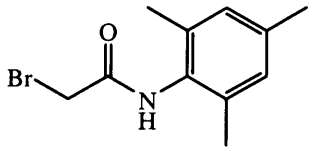
1,2,4-triazole 379[513, 514]



$C_2H_3N_3$
69.0327 g/mol

The *title compound* was prepared by a literature method.[513] 1,2,4-triazole was synthesised by the addition of hydrazine hydrate (1.1 g, 21.0 mmol, 1.0 eq) to a solution of sodium-diformylamide **393** (2.0 g, 21.0 mmol, 1.0 eq) in ethylene glycol/water (10 mL /1 mL, 96%) and H_2SO_4 (conc. 2 mL). The reaction was heated to 160 °C for 4 days, cooled to room temperature and the solvent was removed *via* distillation. The solid was recrystallised from ethanol to give the *title compound* as a white solid (112 mg, 1.6 mmol, 8%) Melting Point 117 °C, lit.[514] 118 – 120 °C **^{1}HNMR** (D_2O, 300MHz): δ 8.42 (2H, s, -N=C*H*N-) **^{13}CNMR** (D_2O, 75.5MHz): δ 147.48 (-N=C*H*N-) **MS (EI)** *m/z* (%): 69 (M^+, 100) **FTIR (ν_{max} cm^{-1})** KBr 3455 (br, NH), 3040 (br), 2950 (br), 2770 (br), 1684 (s), 1274 (s) , 889 (s), 699 (s)

2-bromo-*N*-(2,4,6-trimethylphenyl)-acetamide 380

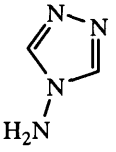


$C_{11}H_{14}BrNO$
255.02588 g/mol

The *title compound* was synthesised by addition of mesitylamine (2.80 mL, 19.8 mmol, 2.0 eq) to a solution of bromoacetylbromide (0.86 mL, 9.9 mmol, 1.0 eq) in DCM (15 mL) at 0°C, after which the reaction was stirred for 2 hours, maintaining the temperature at 0 °C. The organic solution was extracted with water (15 mL x 2) then NH_4Cl (15 mL), followed by washing of the organic phase with brine. The volatiles were removed *in-vacuo* to give the *title compound* as a white amorphous solid (1.84 g,

7.2 mmol, 72%) **Melting Point** 149 – 150 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.19 (6H, s, *o*-ArC$\underline{H}_3$), 2.27 (3H, s, *p*-ArC$\underline{H}_3$), 4.06 (2H, s, -C$\underline{H}_2$Br), 6.90 (2H, s, *m*-ArC$\underline{H}$), 7.26 (1H, br s, N$\underline{H}$) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 18.14 (*o*-Ar$\underline{C}H_3$), 20.93 (*p*-Ar$\underline{C}H_3$), 29.11 (-$\underline{C}H_2$Br), 129.05 (Ar$\underline{C}$H), 130.24 (*o*-Ar$\underline{C}_Q$$CH_3$), 135.06 (*p*-Ar$\underline{C}_Q$$CH_3$), 137.58 (Ar$\underline{C}_Q$NH-), 164.06 (-N$\underline{C}$O-) **HRMS (EI)** *m/z* (%): ($C_{11}H_{14}BrNO$) Requires 255.02587, Found: 255.02539 (60), 176 (35, M-Br), 162 (100, $C_{10}H_{12}NO$), 135 (100, mesityl aniline) **FTIR (ν_{max} cm^{-1})** KBr 3255 (br, NH), 3030 (s), 2965 (s), 2925 (s), 1659 (CO), 1529 (s), 1229 (w), 719 (s, C-Br), 644 (s, C-Br)

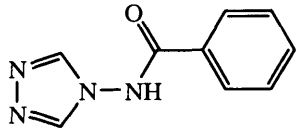
4-amino-1,2,4-triazole 381[515]



$C_2H_4N_4$
84.0436 g/mol

The *title compound* was prepared by a literature method.[515] A solution of formic acid (10.00 mL, 0.26 mol, 1.0 eq), hydrazine sulphate (50.0 g, 0.38 mol, 1.5 eq), and potassium bicarbonate (77.0 g, 0.77 mol, 3.0 eq) in water (250 mL) was heated using a graphite bath at 200 °C, in an open neck flask to permit the continuous elimination of water and excess hydrazine,. The reaction was maintained at 200 °C for 6 hours, cooled to room temperature and extracted with ethanol. The ethanolic extract was filtered and the volatiles were removed *in-vacuo* to afford a crystalline product, which was further purified by recrystallisation from ethanol/ether to give the *title compound* as white plates (10.5 g, 0.12 mol, 48%). **Melting Point** 82 °C, lit.[515] 84 – 86 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 6.36 (2H, br s, -N$\underline{H}_2$), 8.47 (2H, s, 2x -NC$\underline{H}$=N-), **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 144.51 (-N$\underline{C}$H=N-) **MS (EI)** *m/z* (%): 84 (85, M^+) **FTIR (ν_{max} cm^{-1})** KBr 3445 (br, NH), 2970 (br), 2590 (w), 2505 (w), 1964 (s), 1594 (s), 1399 (s), 1219 (s), 1159 (s), 984 (s), 934 (s)

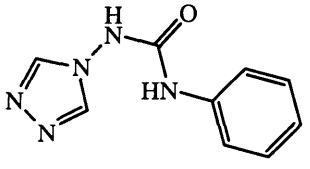
_N_-(_4H_-1,2,4-triazol-4-yl)benzamide 383[516]



$C_9H_8N_4O$
188.06981 g/mol

The *title compound* was synthesised by the addition of benzoic acid (1.21 g, 9.9 mmol, 1.0 eq) and DMAP (120 mg, 1.0 mmol, 0.1 eq) to a solution of 4-amino-1,2,4-triazole **381**, (1.0 g, 11.9 mmol, 1.2 eq) in DCM (5 mL). DCC (2.31 g, 11.0 mmol, 1.1 eq) in DCM (2 mL) was added to the reaction, which was then stirred at room temperature for 12 hours. The reaction was filtered and the collected solid was washed with ethanol (15 mL x 3) and DCM (15 mL x 3) before being dried *in-vacuo* to yield the *title compound* as a white powder (1.20 g, 6.4 mmol, 65%) **Melting Point** >220 °C, lit.[516] 235 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 7.61 (3H, m, ArC*H*), 7.95 (2H, d, ^{3}J=7.4Hz, ArC*H*), 8.81 (2H, s, 2(-N=CHN-)), 12.16 (1H, br s, NH) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 129.48 (ArCH), 132.66 (ArCH), 133.74 (ArCH), 136.04 (ArC_Q), 143.64 (N=CHN), 169.47 (C_QO) **MS (FAB)** *m/z* 189 (100, M+H), 165 (15) **FTIR (ν_{max} cm^{-1}) KBr** 3455 (br, NH), 3045 (br), 2780 (s), 1689 (s, CO), 1519 (s), 1489 (s), 1274 (br), 884 (br) **Elemental analysis** Calculated C 57.44%, H 4.28%, N 29.77%; Found C 57.50%, H 4.30%, N 30.00%

1-phenyl-3-(_4H_-1,2,4-triazol-4-yl)urea 384[517]

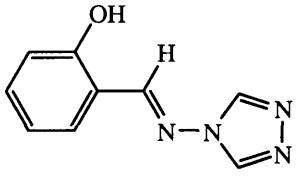


$C_9H_9N_5O$
203.08071 g/mol

The *title compound* was synthesised by addition of phenyl isocyanate (1.83 mL, 16.8 mmol, 1.1 eq) to a solution of 4-amino-1,2,4-triazole **381** (1.25 g, 15.2 mmol, 1.0 eq) in benzene (5 mL). The reaction was stirred at reflux for 1 hour, cooled and left to stand for 1 hour by which time the product had precipitated. The solid was collected *via* filtration, washed in benzene and dried *in-vacuo* to yield a white solid (3.00 g, 14.8 mmol, 97%). **Melting Point** >220 °C, lit.[517] 222 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ

7.01 (1H, t, ^{3}J=7.4Hz, ArC*H*), 7.30 (2H, t, ^{3}J=7.9Hz, ArC*H*), 7.48 (2H, d, ^{3}J=8.0Hz, ArC*H*), 8.69 (2H, s, N=C*H*N), 9.59 (1H, s, N*H*), 9.88 (1H, s, N*H*) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 118.91 (Ar*C*H), 122.75 (N=*C*HN), 128.85 (Ar*C*H), 138.93 (ArC_Q) 144.66 (Ar*C*H), 153.93 (ArC_QO) **MS (EI)** *m/z* 204 (90, M^+H), 407 (100, dimer) **FTIR (ν_{max} cm^{-1}) KBr** 3455 (br, NH), 3045 (br), 2775 (s), 1635 (s, CO), 1519 (s), 1483 (s), 1260 (br), 884 (br) **Elemental analysis** Calculated C 53.20%, H 4.46%, N 34.47%; Found C 53.28%, H 4.58%, N 34.12%

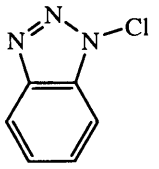
2-(1,2,4-triazol-4-ylimino-methyl)phenol 385



$C_9H_8N_4O$
188.06981 g/mol

The *title compound* was synthesised by the addition of salicaldehyde (1.27 mL, 11.9 mmol, 1.0 eq) to a refluxing solution of 4-amino-1,2,4-triazole **381** (1.0 g, 11.9 mmol, 1.0 eq) in ethanol (5 mL, 99.6%). The reaction solution was maintained at reflux for a further 2 hours. The solution was cooled to room temperature and the product either precipitated spontaneously, and was filtered from the reaction solution, or partial removal of the volatiles *in-vacuo* prompted precipitation. The precipitate was washed with ether, then petroleum spirit to give the *title compound* as a white powder (1.2 g, 6.3 mmol, 54%). **Melting Point** 208 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 6.93 (1H, t, ^{3}J=7.5Hz, ArC*H*), 6.99 (1H, d, ^{3}J=8.3Hz, ArC*H*), 7.41 (1H, dt, ^{3}J=7.5Hz, ^{4}J=1.2Hz, ArC*H*), 7.78 (1H, m, ^{3}J=7.8Hz, ArC*H*), 9.16 (1H, br s, O*H*), 9.18 (2H, s, -NC*H*N-), 10.49 (1H, br s, -N=C*H*-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 116.74 (Ar*C*H), 118.21 (ArC_QOH), 119.67 (Ar*C*H), 127.72 (Ar*C*H), 133.92 (Ar*C*H), 139.01 (-N*C*H=N-), 154.90 (N=*C*H), 158.15 (ArC_QC=N-) **HRMS (EI)** *m/z* (%): ($C_9H_8N_4O$) Requires 188.06981, Found: 188.06946 (85, M^+), 119 (100, $C_7H_5NO^{2-}$) **FTIR (ν_{max} cm^{-1})** KBr 3140 (=NH, s), 3115 (OH, s), 3025 (br), 2715 (br), 2560 (br), 1609 (s), 759 (s) **Elemental analysis** Calculated C 57.44%, H 4.28%, N 29.77%; Found C 57.17%, H 4.30%, N 29.53%

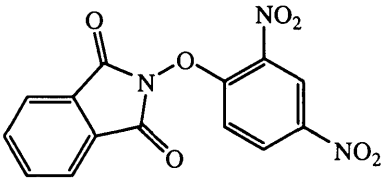
1-Chlorobenzatriazole 386[518]



$C_6H_4ClN_3$
153.00937 g/mol

The *title compound* was prepared by a modified literature method.[518] Benzatriazole (10.0 g, 84.0 mmol, 1.0 eq) was dissolved in aqueous acetic acid (50 mL) followed by slow addition of commercial bleach solution (100 mL) that led to precipitation of the product. The reaction was diluted with water (100 mL), filtered, and the collected solid dissolved in DCM (50 mL), which was dried over sodium sulphate. Recrystallisation of the crude material from DCM/petroleum spirit gave the *title compound* as a white solid (9.2 g, 60.1 mmol, 72%). **Melting point** 102 °C, lit.[518] 104 – 106 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 7.28 (1H, m, ArC*H*), 7.36 (1H, m, ArC*H*), 7.83 (2H, m, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 114.71 (Ar*C*H), 126.43 (Ar*C*H), 132.36 (ArC_Q), 138.20 (ArC_Q) **HRMS (EI)** *m/z* (%) ($C_6H_4ClN_3$) Requires 153.00937, Found: 153.00954 (M^+, $C_6H_4N_3^-$) **FTIR (ν_{max} cm^{-1})** KBr 3085 (br), 3040 (br), 2800 (br), 2290 (br), 1594 (w), 1494 (w), 1199 (s), 749 (s)

N-(2,4-dinitrophenoxy)-phthalimide 387[519, 520]

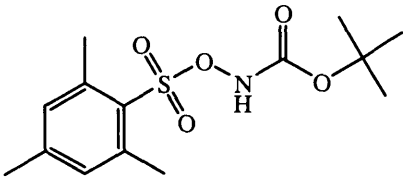


$C_{14}H_7N_3O_7$
329.02840 g/mol

The *title compound* was prepared by a literature method.[519] Freshly distilled triethylamine (21.5 mL, 0.15 mol, 1.0 eq) was added to a suspension of *N*-hydroxyphthalimide (25.0 g, 0.15 mol, 1.0 eq) in acetone (500 mL), and the mixture was stirred at room temperature until it became a homogeneous solution (~10 minutes). During this time the reaction mixture developed a dark red colouration. 2,4-Dinitrochlorobenzene (31.0 g, 0.15 mol, 1.0 eq) was added in a single portion, and the reaction stirred at room temperature for 2 hours. The bright yellow suspension was poured onto ice water (500 mL). The precipitate that formed was collected *via* filtration and washed with cold methanol (100 mL x 3), and petroleum spirit (3 x 100 mL). The

volatiles were removed *in-vacuo* to give the *title compound* as a cream solid (46.55 g, 0.14 mol, 93%) **Melting point** 188 °C, lit.[520] 186 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 7.44 (1H, d, ^{3}J=9.2Hz, ArC*H*), 7.90 (2H, m, Phthalimide ArC*H*), 7.98 (2H, m, Phthalimide ArC*H*), 8.41 (1H, dd, ^{3}J=9.2Hz, ^{4}J 2.7Hz, ArC*H*), 8.95 (1H, d, ^{4}J=2.7Hz, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 114.06 (Ar*C*H), 115.74 (Ar*C*H), 122.62 (Ar*C*H), 124.69 (Ar*C*H), 128.61 (Ar*C*H), 129.49 (ArC_Q-Phthalimide), 135.80 (ArC_Q), 143.12 (ArC_Q), 156.44 (ArC_Q), 162.04 (-C_QO) **MS (EI)** *m/z* (%): 329 (80, M^+) **FTIR (ν_{max} cm^{-1})** film 3260 (s), 3088 (s), 1741 (s), 1600 (s), 1528 (s), 1339 (s), 864 (s)

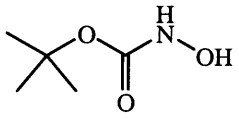
tert-Butyl-_N_-(2,4,6-trimethylphenyl)sulphonyloxycarbamate 388[521, 522]



$C_{14}H_{21}NO_5S$
315.11404 g/mol

The *title compound* was prepared by a literature method.[521] *tert*-Butyl-*N*-hydroxycarbonate **389** (1.5 g, 11.4 mmol, 1.0 eq), and freshly distilled triethylamine (1.59 mL, 11.4 mmol, 1.0 eq) were dissolved in DMF (7.5 mL, anhydrous) at 0°C. Freshly purified (2,4,6-trimethylphenyl)sulphonyl chloride (2.46 g, 11.4 mmol, 1.0 eq) was added portion wise over 30 minutes to the reaction solution, which was stirred for 1 hour. The viscous yellow solution was poured onto ice-water (75 mL), and then extracted into DCM (75 mL x 3). The combined organic phases were washed with water (150 mL x 2), and brine (150 mL). The organic solution was dried over Na_2SO_4, filtered and the volatiles removed *in-vacuo*. The residue was purified by chromatography (eluent: toluene, toluene:ethyl acetate 35:1) to give the *title compound* as white plates (1.86 g, 5.90 mmol, 52%). **Melting Point** 101 – 103 °C, lit.[522] 104 - 105.5 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.29 (9H, s, -C(C*H*$_3$)$_3$), 2.30 (3H, s, *p*-ArC*H*$_3$), 2.65 (6H, s, *o*-ArC*H*$_3$), 6.97 (2H, s, ArC*H*) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 21.05 (*p*-Ar*C*H$_3$), 23.06 (*o*-Ar*C*H$_3$), 27.67 (-C(*C*H$_3$)$_3$), 83.72 (-*C*(CH$_3$)$_3$), 128.47 (ArC_QSO$_2$-), 131.58 (Ar*C*H), 141.87 (*o*-ArC_QCH$_3$), 144.33 (*p*-ArC_QCH$_3$), 154.23 (-*C*O-) **MS (EI)** *m/z* (%): 338 (100, MNa^+), 282 (30) **FTIR (ν_{max} cm^{-1})** KBr 3263 (br), 2890 (br) 1694 (s), 1611 (s), 1596 (s), 1488 (s), 1268 (s), 1192(w), 1120 (w), 937 (s)

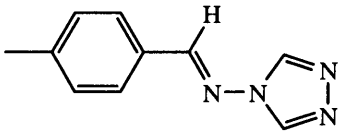
tert-Butyl-_N_-hydroxycarbamate 389[523, 524]



$C_5H_{11}NO_3$
133.07389 g/mol

The *title compound* was prepared by a literature method.[523] A suspension of $NH_2OH.HCl$ (9.60 g, 0.14 mol, 1.5 eq) and K_2CO_3 (19.30 g, 0.14 mol, 1.5 eq) in Et_2O (60 mL) and H_2O (4 mL) was stirred for 1 hour at room temperature with evolution of CO_2. A solution of *tert*-butyl dicarbonate (20.00 g, 70.0 mmol, 1.0 eq) at 0 °C in Et_2O (40 mL) was added dropwise to the reaction solution which was stirred for 12 hours at room temperature. The organic phase was separated from the aqueous layer by decanting, filtered, and the solids were washed with Et_2O (50 mL). The combined organic extracts were concentrated to dryness *in-vacuo* and the solid recrystallised from cyclohexane to give the *title compound* as white needles (9.13 g, 68.6 mmol, 98%) **Melting point** 58 °C, lit.[524] 58 – 59 °C (petroleum ether) **^{1}HNMR** ($CDCl_3$, 300MHz): δ 1.46 (9H, s, -C(C<u>*H*</u>$_3$)$_3$), 7.1-7.5 (2H, br s., -O<u>*H*</u>/-N<u>*H*</u>) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 28.14 (-C(<u>*C*</u>H$_3$)$_3$), 82.79(-<u>*C*</u>$_Q$(CH$_3$)$_3$), 159.11 (<u>*C*</u>$_Q$O).

4-Methylbenzylidene-(1,2,4-triazol-4-yl)amine 390

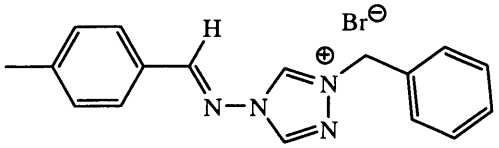


$C_{10}H_{10}N_4$
186.09055 g/mol

The *title compound* was synthesised by reaction of *p*-tolualdehyde (1.4 mL, 11.9 mmol, 1.0 eq) with a refluxing solution of 4-amino-1,2,4-triazole **381** (1.0 g, 11.9 mmol, 1.0 eq) in ethanol (5.0 mL 99.6%). The reaction solution was maintained at reflux for a further 3 hours, during which time the product precipitated. The reaction solution was cooled to room temperature and the precipitate collected *via* filtration. The solid was washed with ether, then petroleum spirit to give the *title compound* as a white powder (1.6 g, 8.5 mmol, 71%). **Melting Point** 128 °C **^{1}HNMR** ($CDCl_3$, 300MHz): δ 2.44 (3H, s, *p*-C<u>*H*</u>$_3$), 7.32 (2H, m, ArC<u>*H*</u>), 7.76 (2H, dd, ^{3}J=6.5Hz, ^{4}J=1.7Hz ArC<u>*H*</u>), 8.64 (1H, s, -N=C<u>*H*</u>-), 8.66 (2H, s, -N=C<u>*H*</u>-N-) **^{13}CNMR** ($CDCl_3$, 75.5MHz): δ 21.67 (*p*-Ar<u>*C*</u>H$_3$), 128.65 (ArC<u>*H*</u>), 128.75 (Ar<u>*C*</u>$_Q$), 129.84 (ArC<u>*H*</u>), 138.17 (-N<u>*C*</u>H=N-), 143.61 (Ar<u>*C*</u>$_Q$),

157.05 (-N=CH-) **HRMS (EI)** *m/z* (%): ($C_{10}H_{10}N_4$) Requires 186.09054, Found: 186.08990 (100, M^+), 104 (95, C_7H_4O) **FTIR** (ν_{max} **cm^{-1}**) KBr 3430 (br, =NH), 3120 (s), 3085 (s), 3040 (s), 2955 (s), 2915 (s), 2320 (br), 1924 (s), 1869 (s), 1614 (s), 1059 (S), 814 (s) **Elemental analysis** Calculated C 52.73%, H 3.90%, N 14.47%; Found C 53.39%, H 4.26%, N 15.25%

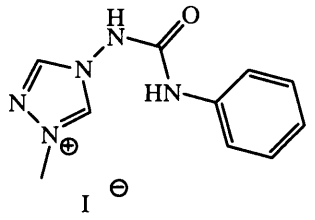
4-(4-methyl-benzylidene-amino)-1-benzyl-*4H*-1,2,4-triazolium bromide 391



$C_{17}H_{17}BrN_4$
356.06366 g/mol

The *title compound* was synthesised by addition of benzyl bromide (345 µl, 2.9 mmol, 1.0 eq) in acetonitrile (1 mL) to a refluxing solution of **390** (500 mg, 2.9 mmol, 1.0 eq) in acetonitrile (10 mL). The reaction solution was maintained at reflux for a further 6 hours, during which time the product precipitated. The reaction solution was cooled to room temperature and the precipitate collected *via* filtration. The solid was washed with ether, then petroleum spirit to give the *title compound* as a white powder (661 mg, 1.9 mmol, 65%) **Melting Point** 195 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 2.41 (3H, s, *p*-ArC*H*$_3$), 5.71 (2H, s, -C*H*$_2$-), 7.41 (5H, m, ArC*H*), 7.53 (2H, m, ArC*H*), 7.84 (2H, d, ^{3}J=7.8Hz, ArC*H*), 9.96 (1H, br s, -N=C*H*-), 11.09 (1H, br s, -N-CH=N$^+$-) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 21.42 (p-ArCH$_3$), 55.23 (-CH$_2$-), 127.97 (ArC$_Q$), 128.83 (ArCH), 128.95 (ArCH), 128.99 (ArCH), 129.37 (ArCH), 130.14 (ArCH), 133.01 (ArC$_Q$), 140.16 (-N=CH-) 144.54 (ArC$_Q$), 164.83 (ArCH) **HRMS (FAB)** *m/z* (%): ($C_{17}H_{17}BrN_4$ +H) Requires 278.15314, Found: 278.15282 (60, M^+H), 175 (25) **FTIR** (ν_{max} **cm^{-1}**) KBr 3434 (br, =NH), 3100 (w), 3030 (s), 2960 (s), 2910 (br), 1609 (s), 1564 (s), 1064 (s), 749 (s)

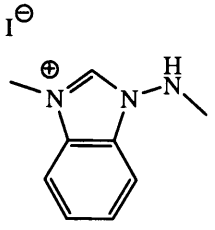
1-phenyl-3-(1-methyl-1,2,4-triazolium)-urea bromide 392[489]



$C_{10}H_{12}IN_5O$
345.00865 g/mol

The *title compound* was synthesised by dissolving N-(*4H*-1,2,4-triazol-4-yl)benzamide **383**, (2.03 g, 10.0 mmol, 1.0 eq) in DMF (3 mL) and diluting further with ethanol (25 mL, 99.6%). The solution was heated to reflux and MeI (12.0 mL, 0.1 mol, 10.0 eq) was added *via* syringe pump over 2 hours. The reaction was stirred at reflux for 8 hours, before cooling to room temperature and collection of the precipitate *via* filtration. The precipitate was washed with EtOAc (25 mL x 2) and dried *in vacuo* to yield a white solid (2.24 g, 6.5 mmol, 65%) **Melting Point** 115 – 116 °C, lit.[489] 117 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 4.14 (3H, s, CH_3), 7.07 (1H, m, ArC*H*), 7.33 (2H, m, ArC*H*), 7.49 (2H, dd, ^{3}J=7.5Hz, ^{4}J=1.2Hz, ArC*H*), 9.54 (1H, s, N=C*H*N), 9.93 (1H, s, N*H*), 10.51 (1H, s, $^+$N=C*H*N), 10.60 (1H, s, N*H*), **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 39.44 (*C*H_3) 113.62 ($^+$N=*C*HN), 119.04 (Ar*C*H), 123.38 (N=*C*HN), 128.98 (Ar*C*H), 138.12 (Ar*C*H), 144.79 (ArC_Q), 153.00 (ArC_QO) **HRMS (EI)** *m/z* (%): ($C_{10}H_{12}IN_5O$ +H-I) Requires 218.10364, Found: 218.10338 (80, M+H-I) **FTIR (ν_{max} cm^{-1})** KBr 3465 (br), 3255 (s), 3200 (s), 3120 (s), 3030 (s), 1719 (CO, s), 1559 (s), 1324 (s), 1069 (s), 769 (s)

1-aminomethyl-3-methyl-benzimidazolium iodide 393

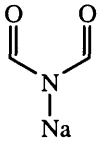


$C_9H_{12}IN_3$
289.00759 g/mol

The *title compound* was synthesised by stirring 1-amino-3-methylbenzimidazolium iodide **340** (250 mg, 0.91 mmol, 1.0 eq) in acetone (3 mL) at room temperature for 144 hours in the presence of K_2CO_3 (125 mg, 0.91 mmol, 1.0 eq) and MeI (0.45 mL, 7.28 mmol, 8.0 eq). The volatiles were removed *in vacuo* and the solid recrystallised from

ethanol to give the *title compound* as a white solid (176 mg, 0.61 mmol, 67%) **Melting Point** 190 – 191 °C **^{1}HNMR** (DMSO-D_6, 300MHz): δ 3.65 (3H, s, -C$\underline{H}_3$), 4.16 (3H, s, -C$\underline{H}_3$), 6.93 (2H, s, -N$\underline{H}_2$), 7.65 (2H, m, ArC$\underline{H}$), 7.92 (2H, m, ArC$\underline{H}$), 10.42 (1H, s, N=C$\underline{H}$N) **^{13}CNMR** (DMSO-D_6, 75.5MHz): δ 34.06 (C$\underline{H}_3$), 39.80 (C$\underline{H}_3$), 112.47 (ArC$\underline{H}$), 113.62 (ArC$\underline{H}$), 127.27 (ArC$\underline{H}$), 127.90 (ArC$\underline{H}$), 130.25 (Ar$\underline{C}_Q$), 131.84 (Ar$\underline{C}_Q$), 144.76 (ArC$\underline{H}$) **HRMS (EI)** *m/z* (%): ($C_9H_{12}IN_3$ -I) Requires 162.10312, Found: 162.10274 (10, M^+-I), 127 (45) FTIR (**ν_{max} cm^{-1}**) **KBr** 3440 (NH, br), 3115 (s), 3060 (s), 3020 (s), 1674 (s), 1559 (s), 1469 (s), 1339 (s), 1059 (s), 749 (s) **Elemental analysis** Calculated C 34.93%, H 3.66 %, N 15.28%, I 46.13%; Found C 34.83%, H 3.74%, N 15.00%, I 45.89%

Sodium diformylamide 394[525]



$C_2H_2NNaO_2$
94.99832 g/mol

The *title compound* was prepared by a literature method.[525] Formamide (90.0 g, 2.0 mol, 2.0 eq) and freshly prepared NaOMe/MeOH (1 M) (23.5 g Na^0 / methanol 200 mL, 1.0 eq) were stirred at room temperature for 1 hour. The volatiles were removed over 2 hours, *in-vacuo*, at 90°C, which gave the *title compound* as a white solid (9.7 g, 1.32 mol, ~100%) **Melting Point** 190 °C (Decomp.) lit. value not given **^{1}HNMR** (D_2O, 300MHz): δ 8.00 (1H, br s, $\underline{H}$CON-), 8.41 (1H, br s, $\underline{H}$CO-) **^{13}CNMR** (D_2O, 75.5MHz): δ 167.18 (H$\underline{C}$ON-), 171.60 (H$\underline{C}$ON-) **MS (CI)** methane *m/z* (%): 95 (20, M^+), 71 (100)

Chapter 10

Appendix

Crystal data and structure refinement for 111

Table 1. Crystal data and structure refinement for **111**

Identification code	**111**	
Empirical formula	$C_{49}H_{48}Cl_6N_5O_{0.50}PRu$	
Formula weight	1059.66	
Temperature	120(2) K	
Wavelength	0.68880 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 20.561(4) Å	α = 90°
	b = 18.024(3) Å	β = 102.444(4)°
	c = 13.845(3) Å	γ = 90°
Volume	5010.3(17) Å^3	
Z	4	
Density (calculated)	1.405 Mg / m^3	
Absorption coefficient	0.705 mm^{-1}	
F(000)	2168	
Crystal	Block; orange	
Crystal size	0.08 × 0.06 × 0.04 mm^3	
θ range for data collection	1.82 – 26.10°	
Index ranges	$0 \le h \le 26$, $-22 \le k \le 0$, $-17 \le l \le 17$	
Reflections collected	25550	
Independent reflections	25553 [R_{int} = 0.0000]	
Completeness to θ = 26.10°	98.9 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	0.9724 and 0.9458	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	25553 / 0 / 577	
Goodness-of-fit on F^2	1.027	
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0806, $wR2$ = 0.2084	
R indices (all data)	$R1$ = 0.1048, $wR2$ = 0.2379	
Largest diff. peak and hole	2.440 and −1.830 e Å^{-3}	

Diffractometer: *Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *asymmetric unit* sphere). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: *SORTAV* (R. H. Blessing, Acta Cryst. A**51** (1995) 33–37; R. H. Blessing, J. Appl. Cryst. **30** (1997) 421–426). **Structure solution**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). **Structure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Cameron - A Molecular Graphics Package. (D. M. Watkin, L. Pearce and C. K. Prout, Chemical Crystallography Laboratory, University of Oxford, 1993).

Special details:
Twinned synchrotron data

Table 2. Atomic coordinates [$\times 10^4$], equivalent isotropic displacement parameters [$Å^2 \times 10^3$] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
C1	387(5)	8618(5)	8971(5)	107(3)	1
C5	1447(2)	7098(3)	11933(3)	43(1)	1
C8	2838(3)	8042(3)	9604(4)	58(2)	1
C18	3469(2)	4844(2)	9239(3)	33(1)	1
C23	2708(3)	3082(2)	7946(5)	58(1)	1
C26	1546(4)	4245(4)	4734(5)	85(2)	1
C29	3318(2)	5684(2)	7036(3)	39(1)	1
C48	640(3)	5966(3)	7311(4)	52(1)	1
C49	4451(5)	7146(5)	6247(7)	109(3)	1
C2	1001(4)	8257(3)	9590(4)	69(2)	1
C3	960(3)	7857(3)	10446(4)	56(1)	1
C4	1508(2)	7492(3)	11001(3)	42(1)	1
C6	2105(3)	7513(2)	10679(3)	38(1)	1
C7	2175(3)	7947(2)	9876(3)	46(1)	1
C9	1607(4)	8314(3)	9344(4)	62(2)	1
C10	2999(2)	6521(2)	10976(3)	29(1)	1
C11	2984(2)	7371(2)	12202(3)	37(1)	1
C12	3497(2)	6930(2)	12546(3)	35(1)	1
C13	3953(2)	5823(2)	11816(3)	32(1)	1
C14	4483(2)	5650(2)	12576(3)	39(1)	1
C15	4891(2)	5058(3)	12431(4)	43(1)	1
C16	4775(2)	4673(2)	11544(4)	40(1)	1
C17	4229(2)	4888(2)	10825(3)	31(1)	1
C19	4363(2)	4039(2)	9460(4)	39(1)	1
C20	4008(2)	3946(2)	8546(4)	40(1)	1
C21	2971(2)	4405(2)	7501(3)	39(1)	1
C22	2614(3)	3737(3)	7247(4)	48(1)	1
C24	2169(3)	3706(3)	6347(5)	62(2)	1
C25	2046(3)	4301(3)	5687(4)	62(2)	1
C27	2421(3)	4940(3)	5964(4)	50(1)	1
C28	2893(2)	5007(2)	6838(3)	39(1)	1
C30	1917(2)	4220(2)	9720(4)	44(1)	1
C31	1681(2)	4341(3)	8718(4)	47(1)	1
C32	1271(3)	3822(3)	8138(5)	60(2)	1
C33	1117(3)	3166(3)	8577(6)	71(2)	1
C34	1360(3)	3037(3)	9553(6)	74(2)	1
C35	1752(3)	3551(3)	10126(5)	63(2)	1
C36	2703(2)	4651(3)	11694(4)	46(1)	1
C37	3100(3)	4042(3)	11791(5)	59(2)	1
C38	3473(3)	3822(3)	12757(5)	58(2)	1

C39	3422(3)	4227(4)	13551(5)	70(2)	1
C40	3033(3)	4850(4)	13472(5)	69(2)	1
C41	2675(3)	5067(3)	12543(4)	53(1)	1
C42	1501(2)	5382(3)	10662(3)	38(1)	1
C43	1187(3)	5037(3)	11350(4)	49(1)	1
C44	541(3)	5253(3)	11393(4)	55(1)	1
C45	203(3)	5771(3)	10746(4)	58(1)	1
C46	512(3)	6099(3)	10073(4)	50(1)	1
C47	1168(2)	5913(3)	10041(3)	40(1)	1
N1	2678(2)	7128(2)	11246(2)	32(1)	1
N2	3506(2)	6403(2)	11803(2)	30(1)	1
N3	3813(2)	5431(2)	10966(3)	28(1)	1
N4	4032(2)	4582(2)	9883(3)	34(1)	1
N5	3457(2)	4426(2)	8412(3)	35(1)	1
P1	2304(1)	5017(1)	10461(1)	35(1)	1
Cl1	2243(1)	6218(1)	8489(1)	32(1)	1
Cl2	3939(1)	6521(1)	9382(1)	31(1)	1
Cl3	489(1)	5338(1)	6323(1)	82(1)	1
Cl4	−50(1)	6526(1)	7295(1)	80(1)	1
Ru1	3053(1)	5734(1)	9890(1)	26(1)	1
Cl6	5043(1)	7396(1)	7273(2)	94(1)	1
Cl5	4723(2)	6429(2)	5447(3)	149(1)	1
O1	6062(4)	7972(4)	9080(5)	58(2)	0.50

Table 3. Bond lengths [Å] and angles [°].

C1–C2	1.512(8)
C1–H1A	0.9800
C1–H1B	0.9800
C1–H1C	0.9800
C5–C4	1.501(6)
C5–H5A	0.9800
C5–H5B	0.9800
C5–H5C	0.9800
C8–C7	1.501(8)
C8–H8A	0.9800
C8–H8B	0.9800
C8–H8C	0.9800
C18–N5	1.366(5)
C18–N4	1.383(6)
C18–Ru1	2.109(4)
C23–C22	1.512(7)
C23–H23A	0.9800
C23–H23B	0.9800
C23–H23C	0.9800
C26–C25	1.491(9)
C26–H26A	0.9800
C26–H26B	0.9800
C26–H26C	0.9800
C29–C28	1.492(6)
C29–H29A	0.9800
C29–H29B	0.9800
C29–H29C	0.9800
C48–Cl4	1.737(6)
C48–Cl3	1.751(6)
C48–H48A	0.9900
C48–H48B	0.9900
C49–Cl6	1.720(10)
C49–Cl5	1.863(9)
C49–H49A	0.9900
C49–H49B	0.9900
C2–C9	1.366(10)
C2–C3	1.405(8)
C3–C4	1.386(7)
C3–H3	0.9500
C4–C6	1.394(7)
C6–C7	1.393(6)
C6–N1	1.445(6)
C7–C9	1.404(8)
C9–H9	0.9500

C10–N1	1.370(5)
C10–N2	1.388(5)
C10–Ru1	2.088(4)
C11–C12	1.324(6)
C11–N1	1.406(5)
C11–H11	0.9500
C12–N2	1.404(5)
C12–H12	0.9500
C13–N3	1.349(5)
C13–C14	1.377(6)
C13–N2	1.389(5)
C14–C15	1.399(6)
C14–H14	0.9500
C15–C16	1.385(7)
C15–H15	0.9500
C16–C17	1.385(6)
C16–H16	0.9500
C17–N3	1.342(5)
C17–N4	1.394(6)
C19–C20	1.329(7)
C19–N4	1.391(5)
C19–H19	0.9500
C20–N5	1.406(5)
C20–H20	0.9500
C21–C28	1.408(6)
C21–C22	1.415(6)
C21–N5	1.431(6)
C22–C24	1.379(8)
C24–C25	1.396(9)
C24–H24	0.9500
C25–C27	1.392(8)
C27–C28	1.384(7)
C27–H27	0.9500
C30–C31	1.385(8)
C30–C35	1.403(6)
C30–P1	1.843(5)
C31–C32	1.393(7)
C31–H31	0.9500
C32–C33	1.396(9)
C32–H32	0.9500
C33–C34	1.357(10)
C33–H33	0.9500
C34–C35	1.363(9)
C34–H34	0.9500
C35–H35	0.9500
C36–C37	1.356(7)
C36–C41	1.406(8)

C36–P1	1.849(5)
C37–C38	1.447(8)
C37–H37	0.9500
C38–C39	1.342(9)
C38–H38	0.9500
C39–C40	1.370(9)
C39–H39	0.9500
C40–C41	1.393(8)
C40–H40	0.9500
C41–H41	0.9500
C42–C47	1.368(7)
C42–C43	1.407(6)
C42–P1	1.852(5)
C43–C44	1.397(7)
C43–H43	0.9500
C44–C45	1.374(8)
C44–H44	0.9500
C45–C46	1.370(8)
C45–H45	0.9500
C46–C47	1.400(7)
C46–H46	0.9500
C47–H47	0.9500
N3–Ru1	1.989(3)
P1–Ru1	2.2789(11)
Cl1–Ru1	2.4306(11)
Cl2–Ru1	2.5261(10)

C2–C1–H1A	109.5
C2–C1–H1B	109.5
H1A–C1–H1B	109.5
C2–C1–H1C	109.5
H1A–C1–H1C	109.5
H1B–C1–H1C	109.5
C4–C5–H5A	109.5
C4–C5–H5B	109.5
H5A–C5–H5B	109.5
C4–C5–H5C	109.5
H5A–C5–H5C	109.5
H5B–C5–H5C	109.5
C7–C8–H8A	109.5
C7–C8–H8B	109.5
H8A–C8–H8B	109.5
C7–C8–H8C	109.5
H8A–C8–H8C	109.5
H8B–C8–H8C	109.5
N5–C18–N4	102.3(3)
N5–C18–Ru1	147.3(3)

N4–C18–Ru1	110.1(3)
C22–C23–H23A	109.5
C22–C23–H23B	109.5
H23A–C23–H23B	109.5
C22–C23–H23C	109.5
H23A–C23–H23C	109.5
H23B–C23–H23C	109.5
C25–C26–H26A	109.5
C25–C26–H26B	109.5
H26A–C26–H26B	109.5
C25–C26–H26C	109.5
H26A–C26–H26C	109.5
H26B–C26–H26C	109.5
C28–C29–H29A	109.5
C28–C29–H29B	109.5
H29A–C29–H29B	109.5
C28–C29–H29C	109.5
H29A–C29–H29C	109.5
H29B–C29–H29C	109.5
Cl4–C48–Cl3	111.0(3)
Cl4–C48–H48A	109.4
Cl3–C48–H48A	109.4
Cl4–C48–H48B	109.4
Cl3–C48–H48B	109.4
H48A–C48–H48B	108.0
Cl6–C49–Cl5	115.0(5)
Cl6–C49–H49A	108.5
Cl5–C49–H49A	108.5
Cl6–C49–H49B	108.5
Cl5–C49–H49B	108.5
H49A–C49–H49B	107.5
C9–C2–C3	118.2(5)
C9–C2–C1	121.4(6)
C3–C2–C1	120.3(7)
C4–C3–C2	121.5(6)
C4–C3–H3	119.3
C2–C3–H3	119.3
C3–C4–C6	118.5(4)
C3–C4–C5	119.5(5)
C6–C4–C5	122.0(4)
C7–C6–C4	121.3(4)
C7–C6–N1	119.4(4)
C4–C6–N1	119.0(4)
C6–C7–C9	117.8(5)
C6–C7–C8	121.3(5)
C9–C7–C8	120.8(5)
C2–C9–C7	122.3(5)

C2–C9–H9	118.9
C7–C9–H9	118.9
N1–C10–N2	102.5(3)
N1–C10–Ru1	147.4(3)
N2–C10–Ru1	110.0(3)
C12–C11–N1	108.1(4)
C12–C11–H11	125.9
N1–C11–H11	125.9
C11–C12–N2	106.1(4)
C11–C12–H12	126.9
N2–C12–H12	126.9
N3–C13–C14	122.2(4)
N3–C13–N2	111.4(4)
C14–C13–N2	126.3(4)
C13–C14–C15	117.6(4)
C13–C14–H14	121.2
C15–C14–H14	121.2
C16–C15–C14	121.0(4)
C16–C15–H15	119.5
C14–C15–H15	119.5
C17–C16–C15	117.1(4)
C17–C16–H16	121.5
C15–C16–H16	121.5
N3–C17–C16	122.8(4)
N3–C17–N4	111.1(4)
C16–C17–N4	126.1(4)
C20–C19–N4	105.7(4)
C20–C19–H19	127.1
N4–C19–H19	127.1
C19–C20–N5	108.0(4)
C19–C20–H20	126.0
N5–C20–H20	126.0
C28–C21–C22	120.9(4)
C28–C21–N5	120.9(4)
C22–C21–N5	117.9(4)
C24–C22–C21	117.8(5)
C24–C22–C23	121.0(5)
C21–C22–C23	121.2(5)
C22–C24–C25	123.6(5)
C22–C24–H24	118.2
C25–C24–H24	118.2
C27–C25–C24	116.3(5)
C27–C25–C26	122.3(6)
C24–C25–C26	121.4(5)
C28–C27–C25	123.8(5)
C28–C27–H27	118.1
C25–C27–H27	118.1

C27–C28–C21	117.5(4)
C27–C28–C29	120.4(4)
C21–C28–C29	122.0(4)
C31–C30–C35	118.2(5)
C31–C30–P1	116.9(3)
C35–C30–P1	124.1(5)
C30–C31–C32	120.7(5)
C30–C31–H31	119.7
C32–C31–H31	119.7
C33–C32–C31	118.9(6)
C33–C32–H32	120.5
C31–C32–H32	120.5
C34–C33–C32	120.6(6)
C34–C33–H33	119.7
C32–C33–H33	119.7
C33–C34–C35	120.5(6)
C33–C34–H34	119.7
C35–C34–H34	119.7
C34–C35–C30	121.0(6)
C34–C35–H35	119.5
C30–C35–H35	119.5
C37–C36–C41	118.7(5)
C37–C36–P1	121.2(5)
C41–C36–P1	119.4(4)
C36–C37–C38	120.1(6)
C36–C37–H37	120.0
C38–C37–H37	120.0
C39–C38–C37	119.2(5)
C39–C38–H38	120.4
C37–C38–H38	120.4
C38–C39–C40	121.9(6)
C38–C39–H39	119.1
C40–C39–H39	119.1
C39–C40–C41	119.1(7)
C39–C40–H40	120.4
C41–C40–H40	120.4
C40–C41–C36	121.0(6)
C40–C41–H41	119.5
C36–C41–H41	119.5
C47–C42–C43	119.5(4)
C47–C42–P1	119.8(3)
C43–C42–P1	119.9(4)
C44–C43–C42	119.1(5)
C44–C43–H43	120.5
C42–C43–H43	120.5
C45–C44–C43	120.8(5)
C45–C44–H44	119.6

C43–C44–H44	119.6
C46–C45–C44	119.6(5)
C46–C45–H45	120.2
C44–C45–H45	120.2
C45–C46–C47	120.6(5)
C45–C46–H46	119.7
C47–C46–H46	119.7
C42–C47–C46	120.2(4)
C42–C47–H47	119.9
C46–C47–H47	119.9
C10–N1–C11	111.2(4)
C10–N1–C6	128.3(3)
C11–N1–C6	120.5(3)
C10–N2–C13	120.2(3)
C10–N2–C12	111.9(3)
C13–N2–C12	127.8(4)
C17–N3–C13	119.1(4)
C17–N3–Ru1	120.9(3)
C13–N3–Ru1	119.7(3)
C18–N4–C19	112.8(4)
C18–N4–C17	120.2(3)
C19–N4–C17	127.0(4)
C18–N5–C20	111.1(4)
C18–N5–C21	129.5(4)
C20–N5–C21	119.3(4)
C30–P1–C36	106.7(2)
C30–P1–C42	94.0(2)
C36–P1–C42	102.8(2)
C30–P1–Ru1	119.39(17)
C36–P1–Ru1	108.89(15)
C42–P1–Ru1	122.78(15)
N3–Ru1–C10	78.56(14)
N3–Ru1–C18	77.68(15)
C10–Ru1–C18	156.08(17)
N3–Ru1–P1	93.77(9)
C10–Ru1–P1	89.43(11)
C18–Ru1–P1	94.83(12)
N3–Ru1–Cl1	171.50(9)
C10–Ru1–Cl1	101.36(11)
C18–Ru1–Cl1	101.72(12)
P1–Ru1–Cl1	94.72(4)
N3–Ru1–Cl2	82.23(9)
C10–Ru1–Cl2	88.39(11)
C18–Ru1–Cl2	85.72(11)
P1–Ru1–Cl2	175.77(4)
Cl1–Ru1–Cl2	89.27(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$]. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + \cdots + 2\,h\,k\,a^*\,b^*\,U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	142(8)	127(6)	40(3)	−3(4)	−8(4)	97(6)
C5	39(3)	63(3)	29(2)	−1(2)	13(2)	10(2)
C8	110(5)	38(2)	37(3)	8(2)	43(3)	14(3)
C18	37(2)	26(2)	40(2)	3(2)	18(2)	5(2)
C23	56(3)	30(2)	86(4)	−8(2)	15(3)	−6(2)
C26	87(5)	93(5)	62(4)	−14(4)	−8(4)	−8(4)
C29	45(3)	36(2)	39(2)	1(2)	19(2)	2(2)
C48	45(3)	53(3)	55(3)	7(2)	6(2)	−4(2)
C49	130(8)	89(5)	123(8)	12(5)	56(7)	38(5)
C2	106(5)	71(4)	25(2)	−5(2)	2(3)	57(4)
C3	65(4)	67(3)	37(3)	−10(2)	11(2)	34(3)
C4	49(3)	56(3)	21(2)	−4(2)	8(2)	19(2)
C6	61(3)	33(2)	22(2)	1(2)	13(2)	18(2)
C7	83(4)	36(2)	25(2)	2(2)	21(2)	22(2)
C9	112(5)	48(3)	26(2)	3(2)	17(3)	34(3)
C10	35(2)	28(2)	27(2)	6(1)	17(2)	1(2)
C11	51(3)	38(2)	27(2)	−2(2)	20(2)	7(2)
C12	40(2)	41(2)	27(2)	−1(2)	17(2)	−1(2)
C13	26(2)	35(2)	37(2)	6(2)	14(2)	2(2)
C14	31(2)	46(2)	38(2)	4(2)	7(2)	1(2)
C15	29(2)	50(3)	50(3)	10(2)	5(2)	4(2)
C16	31(2)	36(2)	55(3)	5(2)	13(2)	5(2)
C17	28(2)	27(2)	41(2)	4(2)	12(2)	1(2)
C19	29(2)	31(2)	62(3)	−5(2)	18(2)	5(2)
C20	36(2)	31(2)	55(3)	−6(2)	17(2)	6(2)
C21	42(3)	35(2)	42(2)	−9(2)	15(2)	3(2)
C22	50(3)	36(2)	58(3)	−13(2)	14(2)	1(2)
C24	66(4)	48(3)	69(4)	−21(3)	7(3)	−7(3)
C25	68(4)	66(3)	50(3)	−18(3)	8(3)	−8(3)
C27	54(3)	58(3)	39(3)	−6(2)	9(2)	1(2)
C28	48(3)	35(2)	36(2)	−6(2)	15(2)	6(2)
C30	32(2)	33(2)	69(3)	7(2)	17(2)	−2(2)
C31	36(3)	37(2)	73(4)	−6(2)	20(2)	−2(2)
C32	44(3)	50(3)	88(4)	−17(3)	16(3)	−7(2)
C33	50(3)	41(3)	119(6)	−13(3)	12(4)	−15(2)
C34	59(4)	45(3)	114(6)	15(3)	12(4)	−12(3)
C35	56(3)	40(3)	93(5)	16(3)	20(3)	−10(2)
C36	31(2)	49(3)	61(3)	24(2)	14(2)	2(2)

C37	36(3)	52(3)	91(4)	31(3)	18(3)	3(2)
C38	45(3)	52(3)	75(4)	27(3)	6(3)	3(2)
C39	60(4)	76(4)	69(4)	30(3)	1(3)	−4(3)
C40	60(4)	91(4)	55(3)	26(3)	11(3)	−2(3)
C41	44(3)	69(3)	45(3)	19(2)	11(2)	−1(2)
C42	33(2)	48(2)	38(2)	−1(2)	17(2)	−6(2)
C43	41(3)	59(3)	49(3)	11(2)	16(2)	−5(2)
C44	41(3)	78(4)	53(3)	4(3)	28(2)	−7(3)
C45	33(3)	84(4)	62(3)	0(3)	21(2)	6(3)
C46	41(3)	61(3)	50(3)	2(2)	12(2)	14(2)
C47	35(2)	53(3)	35(2)	1(2)	14(2)	4(2)
N1	46(2)	32(2)	25(2)	1(1)	19(2)	6(2)
N2	33(2)	33(2)	27(2)	1(1)	11(1)	1(1)
N3	28(2)	22(1)	38(2)	4(1)	14(1)	0(1)
N4	29(2)	28(2)	46(2)	1(1)	13(2)	5(1)
N5	37(2)	26(2)	41(2)	−5(1)	11(2)	3(1)
P1	28(1)	35(1)	44(1)	11(1)	12(1)	0(1)
Cl1	34(1)	34(1)	30(1)	5(1)	13(1)	2(1)
Cl2	35(1)	26(1)	37(1)	−1(1)	19(1)	−1(1)
Cl3	112(2)	60(1)	72(1)	−6(1)	17(1)	−20(1)
Cl4	85(1)	80(1)	83(1)	32(1)	33(1)	34(1)
Ru1	27(1)	24(1)	31(1)	3(1)	13(1)	2(1)
Cl6	69(1)	68(1)	154(2)	4(1)	44(1)	4(1)
Cl5	148(3)	146(2)	153(3)	48(2)	29(2)	68(2)
O1	54(4)	81(5)	39(4)	−21(3)	14(3)	−48(4)

Crystal data and structure refinement for 112

Table 1. Crystal data and structure refinement for **112**.

Identification code	s92	
Empirical formula	$C_{108}H_{116}Cl_8N_{10}P_2Ru_2$ (**112** x2 + CH_2Cl_2 x2)	
Formula weight	2101.79	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pca21	
Unit cell dimensions	a = 17.9597(5) Å	a= 90°
	b = 19.2091(6) Å	b= 90°
	c = 28.7358(10) Å	g = 90°
Volume	9913.6(5) $Å^3$	
Z	4	
Density (calculated)	1.408 Mg/m^3	
Absorption coefficient	0.607 mm^{-1}	
F(000)	4352	
Crystal size	0.06 x 0.04 x 0.01 mm^3	
Theta range for data collection	3.03 to 20.60°.	
Index ranges	-17<=h<=17, -18<=k<=19, -28<=l<=28	
Reflections collected	9624	
Independent reflections	9624 [R(int) = 0.0000]	
Absorption correction	Multi scan	
Max. and min. transmission	1.02039 and 0.95401	
Refinement method	Full-matrix-block least-squares on F^2	
Data / restraints / parameters	9598 / 1 / 1189	
Goodness-of-fit on F^2	1.045	
Final R indices [I>2sigma(I)]	R1 = 0.0458, wR2 = 0.0914	
R indices (all data)	R1 = 0.0693, wR2 = 0.1024	
Absolute structure parameter	0.48(4)	
Extinction coefficient	0.00037(6)	
Largest diff. peak and hole	0.417 and -0.339 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 02SW033. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	619(5)	2697(4)	3379(3)	27(2)
C(2)	132(5)	2692(5)	2947(3)	36(3)
C(3)	680(5)	1974(4)	3581(3)	42(3)
C(4)	1189(5)	5100(4)	4792(3)	40(3)
C(5)	1291(5)	4311(4)	4724(3)	28(2)
C(6)	1235(6)	3937(4)	5195(3)	44(3)
C(7)	908(5)	3536(4)	4042(3)	27(2)
C(8)	378(5)	3229(4)	3747(3)	20(2)
C(9)	-356(5)	3414(4)	3804(3)	26(2)
C(10)	705(5)	4010(4)	4398(3)	21(2)
C(11)	-37(5)	4176(4)	4438(3)	25(2)
C(12)	-569(5)	3889(4)	4146(3)	28(2)
C(13)	2255(5)	3616(4)	3762(3)	30(2)
C(14)	2709(5)	2819(4)	4296(3)	32(2)
C(15)	1967(5)	2831(4)	4348(3)	25(2)
C(16)	3582(5)	3579(4)	3854(3)	26(2)
C(17)	4247(5)	3445(4)	4063(3)	27(2)
C(18)	4842(5)	3840(4)	3960(3)	30(2)
C(19)	4790(5)	4406(4)	3653(3)	26(2)
C(20)	4106(4)	4510(4)	3451(3)	21(2)
C(21)	3193(5)	5054(4)	2962(3)	20(2)
C(22)	4401(5)	5522(4)	2915(3)	29(2)
C(23)	3947(5)	5854(4)	2606(3)	23(2)
C(24)	2615(4)	5891(4)	2395(3)	19(2)
C(25)	2152(5)	6334(4)	2650(3)	20(2)
C(26)	1574(5)	6671(4)	2408(3)	31(2)
C(27)	1450(5)	6561(4)	1942(3)	28(2)
C(28)	1937(5)	6119(4)	1699(3)	28(2)
C(29)	2532(5)	5780(4)	1918(3)	23(2)
C(30)	3060(5)	5330(4)	1626(3)	27(2)
C(31)	3637(5)	5805(5)	1378(3)	42(3)
C(32)	2638(5)	4913(4)	1270(3)	45(3)
C(33)	2283(5)	6499(4)	3147(3)	32(3)
C(34)	1553(5)	6582(4)	3426(3)	39(3)
C(35)	2751(5)	7176(4)	3187(3)	40(3)
C(36)	678(6)	3246(5)	1684(3)	45(3)
C(37)	1052(6)	2663(5)	1822(3)	42(3)
C(38)	1644(5)	2721(5)	2140(3)	34(2)
C(39)	1860(4)	3373(4)	2303(3)	22(2)
C(40)	1468(5)	3962(4)	2152(3)	28(2)
C(41)	889(5)	3903(4)	1842(3)	32(2)
C(42)	2968(6)	2692(4)	2910(3)	28(2)
C(43)	2464(6)	2213(4)	3102(3)	41(3)

C(44)	2702(6)	1644(4)	3346(3)	46(3)
C(45)	3449(7)	1536(5)	3427(4)	55(3)
C(46)	3948(6)	1969(5)	3233(3)	44(3)
C(47)	3725(6)	2555(4)	2977(3)	31(2)
C(48)	3382(5)	3659(4)	2230(3)	24(2)
C(49)	4081(5)	3937(4)	2335(3)	25(2)
C(50)	4642(5)	4005(4)	2001(4)	40(3)
C(51)	4509(6)	3777(4)	1547(3)	35(3)
C(52)	3838(6)	3477(4)	1437(3)	37(3)
C(53)	3277(5)	3416(4)	1772(3)	30(2)
C(60)	6605(5)	9683(4)	2101(3)	30(2)
C(61)	5988(5)	9245(4)	2319(4)	51(3)
C(62)	7034(6)	10064(4)	2499(3)	41(3)
C(63)	7114(5)	9223(4)	1801(3)	22(2)
C(64)	7709(5)	8885(4)	2018(3)	30(2)
C(65)	8151(5)	8428(4)	1770(3)	30(2)
C(66)	8009(5)	8319(4)	1305(3)	32(2)
C(67)	7413(5)	8633(4)	1069(3)	24(2)
C(68)	6995(5)	9106(4)	1333(3)	20(2)
C(69)	7233(5)	8436(4)	575(3)	34(2)
C(70)	6854(5)	7718(4)	580(3)	43(3)
C(71)	7918(5)	8433(4)	256(3)	33(2)
C(72)	5630(5)	9193(4)	1115(3)	23(2)
C(73)	5217(5)	9562(4)	816(3)	21(2)
C(74)	6421(5)	9964(4)	786(3)	21(2)
C(75)	5523(5)	10572(4)	298(3)	17(2)
C(76)	4847(5)	10704(4)	98(3)	25(2)
C(77)	4800(5)	11284(4)	-190(3)	33(2)
C(78)	5436(5)	11693(4)	-291(3)	22(2)
C(79)	6098(5)	11500(4)	-88(3)	21(2)
C(80)	7442(5)	11442(4)	7(3)	17(2)
C(81)	7002(5)	12279(4)	-505(3)	21(2)
C(82)	7728(5)	12259(4)	-539(3)	21(2)
C(83)	8778(5)	11504(4)	-272(3)	23(2)
C(84)	8940(5)	10985(4)	-600(3)	24(2)
C(85)	9664(6)	10788(4)	-628(3)	35(3)
C(86)	10236(6)	11070(4)	-365(3)	35(3)
C(87)	10049(5)	11600(4)	-69(3)	29(2)
C(89)	9311(5)	11831(4)	-16(3)	23(2)
C(90)	9151(5)	12422(4)	311(3)	32(2)
C(92)	9521(6)	13108(4)	141(3)	60(3)
C(93)	8360(5)	10696(4)	-942(3)	37(3)
C(94)	8451(5)	11099(5)	-1406(3)	43(3)
C(95)	8438(6)	9917(4)	-1018(4)	55(3)
C(96)	6265(5)	11361(4)	1529(3)	26(2)
C(97)	5555(5)	11124(4)	1395(3)	27(2)
C(98)	4989(5)	11054(4)	1716(3)	32(2)
C(99)	5112(6)	11240(4)	2170(4)	40(3)
C(100)	5795(6)	11482(4)	2310(3)	35(3)
C(101)	6365(5)	11538(4)	1995(3)	29(2)

C(102)	6797(5)	12330(4)	871(3)	20(2)
C(103)	6073(5)	12526(4)	785(3)	29(2)
C(104)	5914(5)	13128(5)	534(3)	40(3)
C(105)	6491(6)	13543(4)	374(3)	36(3)
C(106)	7215(6)	13365(4)	473(3)	33(2)
C(107)	7369(6)	12762(4)	721(3)	32(2)
C(108)	7833(5)	11559(4)	1474(3)	25(2)
C(109)	8199(5)	10953(4)	1609(3)	31(2)
C(110)	9397(5)	12280(4)	801(3)	45(3)
C(111)	8999(5)	11593(5)	2126(3)	41(3)
C(112)	8617(6)	12200(5)	2001(3)	40(3)
C(113)	8045(5)	12180(4)	1678(3)	28(2)
C(114)	8780(6)	10972(5)	1926(3)	42(3)
C(900)	6243(5)	5808(4)	510(4)	54(3)
C(901)	1015(7)	9518(4)	8725(4)	74(4)
N(1)	1684(4)	3312(3)	4017(2)	20(2)
N(2)	2889(4)	3298(3)	3952(2)	20(2)
N(3)	3516(4)	4093(3)	3537(2)	23(2)
N(4)	3918(4)	5027(3)	3132(2)	21(2)
N(5)	3233(4)	5579(3)	2632(2)	21(2)
N(6)	6365(4)	9445(3)	1098(2)	14(2)
N(7)	5706(4)	10032(3)	611(2)	17(2)
N(8)	6146(4)	10972(3)	228(2)	18(2)
N(9)	6806(4)	11777(3)	-180(2)	20(2)
N(10)	7999(4)	11736(3)	-237(2)	19(2)
Cl(1)	1282(1)	4732(1)	3102(1)	27(1)
Cl(2)	2543(1)	5150(1)	3954(1)	26(1)
Cl(3)	7041(1)	9893(1)	-220(1)	26(1)
Cl(4)	8344(1)	10223(1)	623(1)	27(1)
Cl(5)	5542(2)	5222(1)	707(1)	54(1)
Cl(6)	522(2)	9888(1)	8258(1)	56(1)
Cl(7)	6649(2)	5514(1)	-12(1)	62(1)
Cl(8)	1424(2)	8719(1)	8570(1)	59(1)
Ru(1)	2533(1)	4342(1)	3282(1)	19(1)
Ru(2)	7111(1)	10678(1)	469(1)	19(1)
P(1)	2663(1)	3542(1)	2683(1)	22(1)
P(2)	7028(1)	11450(1)	1090(1)	20(1)

Table 3. Bond lengths [Å] and angles [°] for 02SW033.

C(1)-C(3)	1.508(10)
C(1)-C(2)	1.520(11)
C(1)-C(8)	1.533(10)
C(4)-C(5)	1.539(10)
C(5)-C(10)	1.523(11)
C(5)-C(6)	1.535(11)
C(7)-C(8)	1.406(11)
C(7)-C(10)	1.416(11)
C(7)-N(1)	1.461(8)
C(8)-C(9)	1.374(11)
C(9)-C(12)	1.395(11)
C(10)-C(11)	1.374(11)
C(11)-C(12)	1.385(11)
C(13)-N(1)	1.390(8)
C(13)-N(2)	1.401(9)
C(13)-Ru(1)	2.025(8)
C(14)-C(15)	1.340(11)
C(14)-N(2)	1.389(8)
C(15)-N(1)	1.420(8)
C(16)-N(3)	1.348(7)
C(16)-C(17)	1.363(11)
C(16)-N(2)	1.385(9)
C(17)-C(18)	1.343(11)
C(18)-C(19)	1.404(11)
C(19)-C(20)	1.373(11)
C(20)-N(3)	1.351(8)
C(20)-N(4)	1.393(8)
C(21)-N(5)	1.385(7)
C(21)-N(4)	1.392(8)
C(21)-Ru(1)	2.028(8)
C(22)-C(23)	1.365(11)
C(22)-N(4)	1.430(8)
C(23)-N(5)	1.389(8)
C(24)-C(29)	1.395(11)
C(24)-C(25)	1.398(11)
C(24)-N(5)	1.433(8)
C(25)-C(26)	1.407(11)
C(25)-C(33)	1.481(11)
C(26)-C(27)	1.376(11)
C(27)-C(28)	1.405(11)
C(28)-C(29)	1.402(11)
C(29)-C(30)	1.532(11)
C(30)-C(32)	1.506(11)
C(30)-C(31)	1.553(11)
C(33)-C(34)	1.545(11)
C(33)-C(35)	1.552(11)
C(36)-C(37)	1.364(12)
C(36)-C(41)	1.394(11)

C(37)-C(38)	1.406(12)
C(38)-C(39)	1.392(11)
C(39)-C(40)	1.401(11)
C(39)-P(1)	1.839(8)
C(40)-C(41)	1.374(11)
C(42)-C(47)	1.397(12)
C(42)-C(43)	1.403(12)
C(42)-P(1)	1.844(8)
C(43)-C(44)	1.369(11)
C(44)-C(45)	1.376(13)
C(45)-C(46)	1.344(13)
C(46)-C(47)	1.404(11)
C(48)-C(49)	1.397(11)
C(48)-C(53)	1.409(11)
C(48)-P(1)	1.848(9)
C(49)-C(50)	1.397(11)
C(50)-C(51)	1.397(12)
C(51)-C(52)	1.372(12)
C(52)-C(53)	1.399(12)
C(60)-C(61)	1.525(9)
C(60)-C(63)	1.535(9)
C(60)-C(62)	1.560(8)
C(63)-C(68)	1.382(11)
C(63)-C(64)	1.396(11)
C(64)-C(65)	1.382(11)
C(65)-C(66)	1.377(11)
C(66)-C(67)	1.403(12)
C(67)-C(68)	1.402(11)
C(67)-C(69)	1.506(12)
C(68)-N(6)	1.469(10)
C(69)-C(71)	1.535(11)
C(69)-C(70)	1.538(11)
C(72)-C(73)	1.338(10)
C(72)-N(6)	1.408(10)
C(73)-N(7)	1.390(9)
C(74)-N(6)	1.345(10)
C(74)-N(7)	1.385(10)
C(74)-Ru(2)	2.061(8)
C(75)-C(76)	1.367(11)
C(75)-N(8)	1.374(10)
C(75)-N(7)	1.411(9)
C(76)-C(77)	1.391(11)
C(77)-C(78)	1.416(11)
C(78)-C(79)	1.376(11)
C(79)-N(8)	1.364(9)
C(79)-N(9)	1.403(10)
C(80)-N(10)	1.345(10)
C(80)-N(9)	1.416(10)
C(80)-Ru(2)	2.066(8)
C(81)-C(82)	1.308(11)

C(81)-N(9)	1.389(10)
C(82)-N(10)	1.414(10)
C(83)-C(89)	1.361(11)
C(83)-C(84)	1.402(11)
C(83)-N(10)	1.473(11)
C(84)-C(85)	1.355(12)
C(84)-C(93)	1.537(12)
C(85)-C(86)	1.385(12)
C(86)-C(87)	1.370(11)
C(87)-C(89)	1.406(11)
C(89)-C(90)	1.501(11)
C(90)-C(110)	1.500(12)
C(90)-C(92)	1.555(11)
C(93)-C(95)	1.519(10)
C(93)-C(94)	1.549(12)
C(96)-C(101)	1.394(11)
C(96)-C(97)	1.408(12)
C(96)-P(2)	1.869(9)
C(97)-C(98)	1.380(12)
C(98)-C(99)	1.371(12)
C(99)-C(100)	1.372(12)
C(100)-C(101)	1.371(12)
C(102)-C(103)	1.376(11)
C(102)-C(107)	1.390(11)
C(102)-P(2)	1.851(8)
C(103)-C(104)	1.394(11)
C(104)-C(105)	1.386(12)
C(105)-C(106)	1.374(12)
C(106)-C(107)	1.388(11)
C(108)-C(113)	1.384(11)
C(108)-C(109)	1.393(11)
C(108)-P(2)	1.829(9)
C(109)-C(114)	1.385(12)
C(111)-C(114)	1.381(12)
C(111)-C(112)	1.400(12)
C(112)-C(113)	1.383(12)
C(900)-Cl(7)	1.762(10)
C(900)-Cl(5)	1.781(10)
C(901)-Cl(8)	1.758(9)
C(901)-Cl(6)	1.759(10)
N(3)-Ru(1)	1.971(7)
N(8)-Ru(2)	1.949(7)
Cl(1)-Ru(1)	2.424(2)
Cl(2)-Ru(1)	2.478(2)
Cl(3)-Ru(2)	2.492(2)
Cl(4)-Ru(2)	2.422(2)
Ru(1)-P(1)	2.318(2)
Ru(2)-P(2)	2.326(2)

C(3)-C(1)-C(2)	110.4(7)

C(3)-C(1)-C(8)	111.7(6)
C(2)-C(1)-C(8)	113.9(7)
C(10)-C(5)-C(6)	108.6(7)
C(10)-C(5)-C(4)	111.6(7)
C(6)-C(5)-C(4)	110.0(7)
C(8)-C(7)-C(10)	122.1(8)
C(8)-C(7)-N(1)	119.5(7)
C(10)-C(7)-N(1)	118.2(7)
C(9)-C(8)-C(7)	118.0(7)
C(9)-C(8)-C(1)	121.8(8)
C(7)-C(8)-C(1)	120.3(8)
C(8)-C(9)-C(12)	121.1(8)
C(11)-C(10)-C(7)	117.3(7)
C(11)-C(10)-C(5)	122.1(8)
C(7)-C(10)-C(5)	120.6(8)
C(10)-C(11)-C(12)	121.7(8)
C(11)-C(12)-C(9)	119.8(8)
N(1)-C(13)-N(2)	102.2(5)
N(1)-C(13)-Ru(1)	146.2(6)
N(2)-C(13)-Ru(1)	111.4(5)
C(15)-C(14)-N(2)	107.4(7)
C(14)-C(15)-N(1)	106.9(7)
N(3)-C(16)-C(17)	120.8(7)
N(3)-C(16)-N(2)	110.1(6)
C(17)-C(16)-N(2)	128.7(7)
C(18)-C(17)-C(16)	119.5(8)
C(17)-C(18)-C(19)	121.6(8)
C(20)-C(19)-C(18)	115.9(8)
N(3)-C(20)-C(19)	122.6(7)
N(3)-C(20)-N(4)	110.7(6)
C(19)-C(20)-N(4)	126.8(7)
N(5)-C(21)-N(4)	102.6(5)
N(5)-C(21)-Ru(1)	146.1(6)
N(4)-C(21)-Ru(1)	111.3(4)
C(23)-C(22)-N(4)	103.5(7)
C(22)-C(23)-N(5)	109.7(7)
C(29)-C(24)-C(25)	123.0(7)
C(29)-C(24)-N(5)	119.1(7)
C(25)-C(24)-N(5)	117.8(7)
C(24)-C(25)-C(26)	117.4(8)
C(24)-C(25)-C(33)	122.7(8)
C(26)-C(25)-C(33)	119.7(8)
C(27)-C(26)-C(25)	122.0(8)
C(26)-C(27)-C(28)	118.5(8)
C(29)-C(28)-C(27)	122.1(8)
C(24)-C(29)-C(28)	117.0(8)
C(24)-C(29)-C(30)	123.9(7)
C(28)-C(29)-C(30)	119.1(8)
C(32)-C(30)-C(29)	111.2(8)
C(32)-C(30)-C(31)	109.6(7)

C(29)-C(30)-C(31)	109.5(6)
C(25)-C(33)-C(34)	112.8(7)
C(25)-C(33)-C(35)	109.7(7)
C(34)-C(33)-C(35)	109.6(6)
C(37)-C(36)-C(41)	120.9(9)
C(36)-C(37)-C(38)	119.8(9)
C(39)-C(38)-C(37)	119.9(8)
C(38)-C(39)-C(40)	118.9(8)
C(38)-C(39)-P(1)	125.2(7)
C(40)-C(39)-P(1)	115.8(6)
C(41)-C(40)-C(39)	120.9(8)
C(40)-C(41)-C(36)	119.5(8)
C(47)-C(42)-C(43)	116.8(8)
C(47)-C(42)-P(1)	120.3(7)
C(43)-C(42)-P(1)	121.8(7)
C(44)-C(43)-C(42)	121.5(10)
C(43)-C(44)-C(45)	120.7(9)
C(46)-C(45)-C(44)	119.2(9)
C(45)-C(46)-C(47)	121.5(10)
C(42)-C(47)-C(46)	120.1(9)
C(49)-C(48)-C(53)	116.7(8)
C(49)-C(48)-P(1)	121.5(6)
C(53)-C(48)-P(1)	121.6(7)
C(48)-C(49)-C(50)	122.3(8)
C(51)-C(50)-C(49)	119.3(9)
C(52)-C(51)-C(50)	119.8(9)
C(51)-C(52)-C(53)	120.5(9)
C(52)-C(53)-C(48)	121.3(9)
C(61)-C(60)-C(63)	110.2(5)
C(61)-C(60)-C(62)	108.5(5)
C(63)-C(60)-C(62)	112.8(5)
C(68)-C(63)-C(64)	118.5(8)
C(68)-C(63)-C(60)	123.3(7)
C(64)-C(63)-C(60)	118.2(7)
C(65)-C(64)-C(63)	120.4(8)
C(66)-C(65)-C(64)	119.3(8)
C(65)-C(66)-C(67)	123.0(8)
C(68)-C(67)-C(66)	115.3(8)
C(68)-C(67)-C(69)	123.9(8)
C(66)-C(67)-C(69)	120.8(8)
C(63)-C(68)-C(67)	123.3(8)
C(63)-C(68)-N(6)	119.7(7)
C(67)-C(68)-N(6)	116.9(7)
C(67)-C(69)-C(71)	113.1(8)
C(67)-C(69)-C(70)	108.2(7)
C(71)-C(69)-C(70)	110.9(6)
C(73)-C(72)-N(6)	108.4(7)
C(72)-C(73)-N(7)	105.4(7)
N(6)-C(74)-N(7)	104.1(7)
N(6)-C(74)-Ru(2)	146.4(7)

N(7)-C(74)-Ru(2)	109.6(6)
C(76)-C(75)-N(8)	124.0(7)
C(76)-C(75)-N(7)	127.7(8)
N(8)-C(75)-N(7)	108.3(7)
C(75)-C(76)-C(77)	116.9(8)
C(76)-C(77)-C(78)	121.2(9)
C(79)-C(78)-C(77)	117.4(8)
N(8)-C(79)-C(78)	122.6(8)
N(8)-C(79)-N(9)	110.4(7)
C(78)-C(79)-N(9)	127.0(8)
N(10)-C(80)-N(9)	102.3(7)
N(10)-C(80)-Ru(2)	147.8(7)
N(9)-C(80)-Ru(2)	109.5(6)
C(82)-C(81)-N(9)	106.5(7)
C(81)-C(82)-N(10)	108.5(7)
C(89)-C(83)-C(84)	123.1(9)
C(89)-C(83)-N(10)	119.4(7)
C(84)-C(83)-N(10)	117.3(8)
C(85)-C(84)-C(83)	116.0(9)
C(85)-C(84)-C(93)	120.8(8)
C(83)-C(84)-C(93)	123.0(8)
C(84)-C(85)-C(86)	124.7(9)
C(87)-C(86)-C(85)	116.6(9)
C(86)-C(87)-C(89)	122.2(8)
C(83)-C(89)-C(87)	117.3(8)
C(83)-C(89)-C(90)	123.6(8)
C(87)-C(89)-C(90)	119.1(8)
C(110)-C(90)-C(89)	113.2(7)
C(110)-C(90)-C(92)	108.9(8)
C(89)-C(90)-C(92)	111.2(7)
C(95)-C(93)-C(84)	112.6(8)
C(95)-C(93)-C(94)	111.0(8)
C(84)-C(93)-C(94)	107.4(7)
C(101)-C(96)-C(97)	117.3(8)
C(101)-C(96)-P(2)	122.0(7)
C(97)-C(96)-P(2)	120.6(7)
C(98)-C(97)-C(96)	121.0(8)
C(99)-C(98)-C(97)	119.5(9)
C(98)-C(99)-C(100)	120.7(9)
C(101)-C(100)-C(99)	120.1(9)
C(100)-C(101)-C(96)	121.2(9)
C(103)-C(102)-C(107)	118.7(7)
C(103)-C(102)-P(2)	121.5(7)
C(107)-C(102)-P(2)	119.0(6)
C(102)-C(103)-C(104)	121.0(8)
C(105)-C(104)-C(103)	119.7(8)
C(106)-C(105)-C(104)	119.8(8)
C(105)-C(106)-C(107)	120.2(9)
C(106)-C(107)-C(102)	120.7(9)
C(113)-C(108)-C(109)	118.2(8)

C(113)-C(108)-P(2)	124.9(7)
C(109)-C(108)-P(2)	116.4(6)
C(114)-C(109)-C(108)	121.2(8)
C(114)-C(111)-C(112)	118.2(8)
C(113)-C(112)-C(111)	120.9(8)
C(112)-C(113)-C(108)	120.8(8)
C(111)-C(114)-C(109)	120.7(8)
Cl(7)-C(900)-Cl(5)	111.2(5)
Cl(8)-C(901)-Cl(6)	111.7(6)
C(13)-N(1)-C(15)	111.3(5)
C(13)-N(1)-C(7)	127.3(5)
C(15)-N(1)-C(7)	120.0(5)
C(16)-N(2)-C(14)	127.7(5)
C(16)-N(2)-C(13)	118.8(5)
C(14)-N(2)-C(13)	112.1(5)
C(16)-N(3)-C(20)	119.3(5)
C(16)-N(3)-Ru(1)	120.5(4)
C(20)-N(3)-Ru(1)	119.3(4)
C(21)-N(4)-C(20)	119.0(5)
C(21)-N(4)-C(22)	112.9(5)
C(20)-N(4)-C(22)	127.8(5)
C(21)-N(5)-C(23)	111.3(5)
C(21)-N(5)-C(24)	126.1(5)
C(23)-N(5)-C(24)	121.9(5)
C(74)-N(6)-C(72)	110.3(7)
C(74)-N(6)-C(68)	125.3(7)
C(72)-N(6)-C(68)	123.6(6)
C(74)-N(7)-C(73)	111.8(7)
C(74)-N(7)-C(75)	121.1(7)
C(73)-N(7)-C(75)	126.8(7)
C(79)-N(8)-C(75)	117.5(7)
C(79)-N(8)-Ru(2)	120.6(6)
C(75)-N(8)-Ru(2)	120.7(5)
C(81)-N(9)-C(79)	128.3(7)
C(81)-N(9)-C(80)	111.4(7)
C(79)-N(9)-C(80)	119.2(7)
C(80)-N(10)-C(82)	111.2(7)
C(80)-N(10)-C(83)	128.0(7)
C(82)-N(10)-C(83)	120.0(7)
N(3)-Ru(1)-C(13)	78.4(2)
N(3)-Ru(1)-C(21)	79.0(2)
C(13)-Ru(1)-C(21)	156.4(3)
N(3)-Ru(1)-P(1)	91.5(2)
C(13)-Ru(1)-P(1)	94.2(2)
C(21)-Ru(1)-P(1)	93.0(2)
N(3)-Ru(1)-Cl(1)	169.9(2)
C(13)-Ru(1)-Cl(1)	97.4(2)
C(21)-Ru(1)-Cl(1)	103.7(2)
P(1)-Ru(1)-Cl(1)	98.02(8)
N(3)-Ru(1)-Cl(2)	81.7(2)

C(13)-Ru(1)-Cl(2)	84.3(2)
C(21)-Ru(1)-Cl(2)	85.8(2)
P(1)-Ru(1)-Cl(2)	173.15(8)
Cl(1)-Ru(1)-Cl(2)	88.81(7)
N(8)-Ru(2)-C(74)	79.3(3)
N(8)-Ru(2)-C(80)	79.7(3)
C(74)-Ru(2)-C(80)	158.4(3)
N(8)-Ru(2)-P(2)	91.8(2)
C(74)-Ru(2)-P(2)	92.7(2)
C(80)-Ru(2)-P(2)	93.4(2)
N(8)-Ru(2)-Cl(4)	169.2(2)
C(74)-Ru(2)-Cl(4)	103.3(2)
C(80)-Ru(2)-Cl(4)	96.4(2)
P(2)-Ru(2)-Cl(4)	98.48(8)
N(8)-Ru(2)-Cl(3)	81.3(2)
C(74)-Ru(2)-Cl(3)	85.3(2)
C(80)-Ru(2)-Cl(3)	86.2(2)
P(2)-Ru(2)-Cl(3)	173.02(8)
Cl(4)-Ru(2)-Cl(3)	88.48(7)
C(39)-P(1)-C(42)	106.7(4)
C(39)-P(1)-C(48)	98.7(4)
C(42)-P(1)-C(48)	98.5(4)
C(39)-P(1)-Ru(1)	118.7(2)
C(42)-P(1)-Ru(1)	110.8(2)
C(48)-P(1)-Ru(1)	120.8(2)
C(108)-P(2)-C(102)	106.1(4)
C(108)-P(2)-C(96)	100.6(4)
C(102)-P(2)-C(96)	98.5(4)
C(108)-P(2)-Ru(2)	119.0(3)
C(102)-P(2)-Ru(2)	109.6(3)
C(96)-P(2)-Ru(2)	120.4(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x 10^3)for 02SW033.
The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	27(6)	31(5)	22(6)	-7(4)	1(4)	-2(4)
C(2)	39(7)	42(6)	28(6)	-9(4)	5(5)	0(5)
C(3)	52(7)	29(5)	46(7)	0(5)	21(5)	-5(5)
C(4)	35(7)	32(5)	54(7)	-11(5)	26(5)	-3(5)
C(5)	37(6)	30(5)	18(5)	-8(4)	10(5)	-10(5)
C(6)	53(8)	51(6)	28(6)	-8(5)	3(5)	-12(5)
C(7)	23(6)	24(5)	35(6)	20(5)	9(5)	-4(5)
C(8)	21(6)	25(5)	12(5)	11(4)	14(4)	-5(5)
C(9)	13(6)	38(5)	28(6)	2(5)	8(4)	-9(5)
C(10)	23(6)	30(5)	9(5)	0(4)	-5(4)	-4(5)
C(11)	16(6)	30(5)	30(6)	-5(4)	-5(5)	4(5)
C(12)	16(6)	30(5)	36(6)	14(5)	12(5)	7(5)
C(13)	30(6)	27(5)	33(6)	-10(4)	2(5)	-11(4)
C(14)	32(7)	36(5)	28(6)	1(4)	-15(5)	0(5)
C(15)	26(7)	28(5)	23(5)	2(4)	-5(5)	6(4)
C(16)	30(6)	24(5)	24(5)	10(4)	3(5)	8(4)
C(17)	27(6)	26(5)	27(6)	16(4)	-6(5)	1(5)
C(18)	24(6)	40(6)	27(6)	-5(5)	-8(5)	6(5)
C(19)	23(6)	32(5)	24(5)	6(5)	-1(5)	0(4)
C(20)	10(5)	32(5)	21(5)	3(4)	3(4)	6(4)
C(21)	23(6)	19(5)	17(5)	5(4)	0(4)	6(4)
C(22)	23(6)	27(5)	37(6)	-2(4)	15(5)	-15(5)
C(23)	23(6)	20(5)	26(5)	3(4)	1(5)	-6(4)
C(24)	25(6)	8(4)	24(6)	4(4)	0(5)	-2(4)
C(25)	29(6)	17(5)	15(5)	3(4)	-5(5)	-8(4)
C(26)	29(6)	28(5)	37(7)	7(5)	15(5)	-5(5)
C(27)	21(6)	36(5)	27(6)	6(5)	2(5)	2(5)
C(28)	36(7)	28(5)	20(5)	-1(5)	4(5)	-17(5)
C(29)	26(6)	14(4)	29(6)	11(4)	-15(5)	-2(4)
C(30)	35(7)	26(5)	20(5)	-8(5)	0(5)	18(5)
C(31)	36(7)	56(6)	35(6)	1(5)	14(5)	1(5)
C(32)	57(8)	43(6)	35(6)	-4(5)	0(5)	-1(5)
C(33)	37(7)	16(5)	43(7)	5(4)	7(5)	6(4)
C(34)	44(7)	38(5)	34(6)	-19(5)	6(5)	-11(5)
C(35)	44(7)	58(6)	18(6)	-15(5)	-4(5)	0(5)
C(36)	30(7)	55(7)	51(7)	-19(6)	-11(5)	9(6)
C(37)	31(7)	48(6)	47(7)	-17(5)	21(6)	-6(6)
C(38)	19(6)	41(6)	41(6)	-8(5)	-2(5)	1(5)
C(39)	12(5)	37(5)	18(5)	-12(5)	6(4)	-5(5)
C(40)	34(7)	36(6)	15(5)	-10(4)	-11(5)	-6(5)
C(41)	26(6)	38(6)	32(6)	-8(5)	-10(5)	16(5)
C(42)	42(7)	26(5)	15(5)	-4(4)	-1(5)	5(5)
C(43)	48(7)	19(5)	56(7)	1(5)	18(6)	1(6)

C(44)	66(9)	34(6)	37(7)	18(5)	11(6)	4(6)
C(45)	76(10)	38(6)	50(8)	15(5)	1(7)	25(7)
C(46)	50(7)	39(6)	44(7)	1(6)	-2(6)	22(6)
C(47)	34(7)	28(6)	31(6)	-9(4)	-7(5)	-2(5)
C(48)	34(7)	10(4)	27(6)	1(4)	-5(5)	10(4)
C(49)	19(6)	29(5)	27(6)	-2(4)	-3(5)	4(5)
C(50)	28(7)	33(6)	59(8)	-8(5)	21(6)	7(5)
C(51)	55(8)	27(5)	21(6)	9(5)	14(5)	11(5)
C(52)	49(8)	18(5)	44(7)	-2(5)	1(6)	-16(5)
C(53)	37(7)	23(5)	29(6)	5(5)	11(5)	-1(5)
C(60)	37(7)	26(5)	26(6)	-2(4)	-13(5)	-5(5)
C(61)	57(8)	42(6)	56(8)	-11(5)	8(6)	14(6)
C(62)	74(8)	28(5)	21(6)	-1(4)	-3(5)	7(5)
C(63)	23(6)	14(4)	29(6)	9(4)	4(5)	-1(4)
C(64)	40(7)	33(5)	16(5)	4(5)	-3(5)	-4(5)
C(65)	31(7)	24(5)	35(7)	16(5)	-4(5)	-11(5)
C(66)	22(6)	32(5)	43(7)	5(5)	4(5)	11(5)
C(67)	20(6)	15(5)	38(6)	6(5)	16(5)	-2(4)
C(68)	10(6)	28(5)	20(6)	6(5)	-6(5)	-5(4)
C(69)	46(7)	22(5)	33(6)	-12(4)	-4(5)	-2(5)
C(70)	44(7)	43(6)	43(7)	-15(5)	1(5)	7(5)
C(71)	25(6)	31(5)	42(6)	-3(5)	1(5)	-2(5)
C(72)	21(6)	16(5)	30(6)	4(4)	9(5)	-5(5)
C(73)	20(5)	23(5)	19(5)	4(5)	5(5)	3(5)
C(74)	18(6)	24(5)	21(5)	-5(5)	8(5)	12(4)
C(75)	29(7)	14(5)	7(5)	-7(4)	1(4)	8(5)
C(76)	20(6)	23(5)	32(6)	-5(5)	5(5)	-6(5)
C(77)	38(7)	39(6)	22(6)	7(5)	-4(5)	1(5)
C(78)	26(6)	15(5)	25(5)	3(4)	2(5)	0(5)
C(79)	30(7)	13(5)	20(6)	-1(4)	-9(5)	1(5)
C(80)	19(6)	15(5)	16(5)	-9(4)	-1(5)	-2(5)
C(81)	24(7)	24(5)	14(5)	9(4)	6(4)	10(5)
C(82)	27(7)	15(5)	20(5)	6(4)	7(5)	4(4)
C(83)	33(7)	13(5)	22(6)	3(5)	10(5)	6(5)
C(84)	22(6)	13(5)	38(6)	10(5)	6(5)	5(5)
C(85)	55(8)	26(6)	24(6)	-6(4)	19(6)	2(6)
C(86)	42(7)	29(6)	35(6)	3(5)	2(6)	9(5)
C(87)	31(7)	31(5)	25(6)	6(5)	-20(5)	-1(5)
C(89)	18(6)	29(5)	21(5)	3(4)	-6(5)	-1(5)
C(90)	25(6)	41(6)	31(6)	-3(5)	0(5)	5(5)
C(92)	112(11)	27(6)	42(7)	-4(5)	2(7)	-11(6)
C(93)	27(6)	43(6)	39(6)	-14(5)	11(5)	-4(5)
C(94)	36(7)	61(6)	32(6)	-14(5)	2(5)	-6(5)
C(95)	56(8)	32(6)	78(8)	-23(6)	3(7)	-6(5)
C(96)	37(7)	21(5)	21(6)	5(4)	4(5)	14(5)
C(97)	25(6)	31(5)	25(6)	-10(4)	-8(5)	10(5)
C(98)	20(6)	37(6)	38(7)	-8(5)	7(5)	-7(5)
C(99)	24(7)	43(6)	54(8)	-9(5)	19(6)	0(5)
C(100)	43(8)	38(6)	23(6)	-2(5)	2(6)	15(6)
C(101)	34(7)	23(5)	28(6)	-1(4)	2(5)	5(5)

C(102)	23(6)	24(5)	12(5)	1(4)	4(4)	9(5)
C(103)	35(7)	25(5)	26(5)	5(5)	-1(5)	7(5)
C(104)	36(7)	42(6)	40(6)	-14(6)	-6(6)	25(6)
C(105)	71(9)	17(5)	20(6)	2(4)	-13(6)	-3(6)
C(106)	47(7)	22(5)	29(6)	-14(5)	-5(6)	-7(5)
C(107)	62(8)	22(5)	12(5)	-5(5)	3(5)	7(5)
C(108)	37(6)	19(5)	20(5)	6(4)	-11(5)	-1(5)
C(109)	44(7)	22(5)	28(6)	-1(4)	-7(5)	-1(5)
C(110)	42(7)	44(6)	49(7)	-18(5)	-5(6)	6(5)
C(111)	27(6)	65(7)	31(6)	-4(6)	-25(5)	9(6)
C(112)	40(7)	45(7)	34(6)	-22(5)	-15(6)	-9(6)
C(113)	31(7)	20(5)	32(6)	-3(5)	11(5)	-8(5)
C(114)	52(8)	35(6)	40(6)	-10(5)	-19(6)	12(5)
C(900)	48(7)	49(6)	65(8)	-15(6)	-9(7)	5(5)
C(901)	130(12)	33(6)	58(8)	-16(6)	-38(8)	40(7)
N(1)	10(5)	22(4)	27(4)	-6(4)	3(4)	-4(3)
N(2)	26(5)	23(4)	13(4)	11(3)	-4(4)	-10(4)
N(3)	7(5)	23(4)	37(5)	-8(4)	2(4)	2(3)
N(4)	15(5)	29(4)	18(4)	0(4)	-3(3)	5(3)
N(5)	14(5)	23(4)	24(4)	-4(3)	-2(4)	-3(3)
N(6)	10(5)	13(4)	18(4)	1(3)	8(4)	-9(3)
N(7)	14(5)	17(4)	19(5)	3(4)	2(4)	-1(4)
N(8)	18(5)	25(4)	11(4)	-2(4)	2(3)	3(4)
N(9)	17(5)	28(4)	14(4)	3(4)	2(4)	1(4)
N(10)	22(6)	14(4)	22(5)	-10(4)	1(4)	-3(4)
Cl(1)	22(2)	30(1)	29(1)	-4(1)	0(1)	3(1)
Cl(2)	29(2)	24(1)	24(1)	-2(1)	4(1)	-1(1)
Cl(3)	29(2)	24(1)	25(1)	-2(1)	2(1)	-2(1)
Cl(4)	18(1)	30(1)	33(2)	-3(1)	-2(1)	5(1)
Cl(5)	46(2)	63(2)	53(2)	-14(2)	5(2)	-9(1)
Cl(6)	61(2)	48(2)	59(2)	1(2)	-16(2)	8(1)
Cl(7)	62(2)	69(2)	56(2)	21(2)	0(2)	-11(2)
Cl(8)	53(2)	44(2)	80(2)	3(2)	-6(2)	12(1)
Ru(1)	17(1)	19(1)	19(1)	1(1)	0(1)	0(1)
Ru(2)	18(1)	18(1)	22(1)	0(1)	0(1)	0(1)
P(1)	22(2)	19(1)	25(2)	5(1)	1(1)	2(1)
P(2)	22(2)	18(1)	21(2)	-1(1)	-1(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 02SW033.

H(1)	1131(5)	2834(4)	3276(3)	32
H(2A)	342(16)	2370(20)	2717(7)	55
H(2B)	111(23)	3161(7)	2814(10)	55
H(2C)	-372(9)	2541(24)	3031(4)	55
H(3A)	189(8)	1821(12)	3688(17)	63
H(3B)	1028(23)	1979(7)	3843(12)	63
H(3C)	863(29)	1654(7)	3341(6)	63
H(4A)	1584(18)	5278(6)	4994(15)	60
H(4B)	703(13)	5190(4)	4935(18)	60
H(4C)	1215(31)	5333(5)	4489(4)	60
H(5)	1795(5)	4223(4)	4589(3)	34
H(6A)	1635(18)	4099(20)	5400(7)	66
H(6B)	1282(29)	3434(5)	5148(4)	66
H(6C)	752(12)	4040(21)	5338(8)	66
H(9)	-724(5)	3215(4)	3607(3)	32
H(11)	-189(5)	4496(4)	4671(3)	31
H(12)	-1077(5)	4016(4)	4179(3)	33
H(14)	3049(5)	2534(4)	4463(3)	39
H(15)	1685(5)	2568(4)	4565(3)	31
H(17)	4290(5)	3076(4)	4281(3)	32
H(18)	5309(5)	3734(4)	4098(3)	36
H(19)	5204(5)	4700(4)	3588(3)	31
H(22)	4915(5)	5601(4)	2973(3)	35
H(23)	4096(5)	6219(4)	2402(3)	28
H(26)	1260(5)	6985(4)	2572(3)	37
H(27)	1045(5)	6780(4)	1787(3)	34
H(28)	1860(5)	6047(4)	1375(3)	34
H(30)	3331(5)	5003(4)	1837(3)	32
H(31A)	3876(21)	6109(19)	1607(4)	64
H(31B)	3383(7)	6090(20)	1144(13)	64
H(31C)	4015(17)	5515(5)	1227(16)	64
H(32A)	2975(8)	4579(19)	1122(13)	68
H(32B)	2433(26)	5227(5)	1033(11)	68
H(32C)	2230(18)	4662(22)	1423(4)	68
H(33)	2576(5)	6110(4)	3287(3)	39
H(34A)	1303(14)	7013(14)	3333(12)	58
H(34B)	1668(6)	6600(25)	3759(3)	58
H(34C)	1226(12)	6184(14)	3364(13)	58
H(35A)	2843(24)	7281(15)	3515(3)	60
H(35B)	2478(13)	7563(7)	3044(15)	60
H(35C)	3227(13)	7113(10)	3025(15)	60
H(36)	267(6)	3203(5)	1478(3)	54
H(37)	913(6)	2220(5)	1704(3)	51
H(38)	1897(5)	2315(5)	2244(3)	40
H(40)	1603(5)	4408(4)	2267(3)	34

H(41)	636(5)	4307(4)	1735(3)	38
H(43)	1945(6)	2287(4)	3061(3)	49
H(44)	2348(6)	1320(4)	3462(3)	55
H(45)	3609(7)	1160(5)	3617(4)	66
H(46)	4465(6)	1875(5)	3269(3)	53
H(47)	4088(6)	2860(4)	2850(3)	37
H(49)	4178(5)	4085(4)	2644(3)	30
H(50)	5108(5)	4204(4)	2082(4)	48
H(51)	4882(6)	3829(4)	1315(3)	41
H(52)	3754(6)	3309(4)	1130(3)	44
H(53)	2816(5)	3208(4)	1689(3)	35
H(60)	6371(5)	10042(4)	1896(3)	36
H(61A)	5693(21)	9536(9)	2531(16)	77
H(61B)	6209(5)	8858(18)	2493(17)	77
H(61C)	5665(19)	9061(24)	2073(4)	77
H(62A)	6701(10)	10400(19)	2650(12)	62
H(62B)	7463(17)	10310(22)	2368(4)	62
H(62C)	7205(26)	9722(5)	2728(10)	62
H(64)	7810(5)	8970(4)	2337(3)	36
H(65)	8550(5)	8191(4)	1920(3)	36
H(66)	8329(5)	8017(4)	1136(3)	39
H(69)	6869(5)	8783(4)	450(3)	40
H(70A)	6726(26)	7583(13)	260(4)	65
H(70B)	6399(17)	7741(8)	768(15)	65
H(70C)	7194(12)	7373(7)	713(17)	65
H(71A)	7757(5)	8404(24)	-69(3)	49
H(71B)	8233(14)	8031(14)	331(11)	49
H(71C)	8202(15)	8863(12)	303(12)	49
H(72)	5456(5)	8823(4)	1306(3)	27
H(73)	4699(5)	9514(4)	757(3)	25
H(76)	4428(5)	10413(4)	153(3)	30
H(77)	4333(5)	11407(4)	-322(3)	40
H(78)	5406(5)	12087(4)	-490(3)	26
H(81)	6674(5)	12578(4)	-670(3)	25
H(82)	8024(5)	12548(4)	-734(3)	25
H(85)	9787(6)	10432(4)	-844(3)	42
H(86)	10732(6)	10903(4)	-389(3)	42
H(87)	10431(5)	11819(4)	107(3)	35
H(90)	8600(5)	12496(4)	316(3)	39
H(92A)	9303(25)	13246(18)	-158(11)	90
H(92B)	10057(8)	13035(10)	103(21)	90
H(92C)	9435(31)	13477(9)	370(11)	90
H(93)	7852(5)	10792(4)	-815(3)	44
H(94A)	8927(14)	10973(21)	-1550(9)	65
H(94B)	8442(29)	11601(5)	-1344(4)	65
H(94C)	8042(16)	10978(21)	-1616(7)	65
H(95A)	8018(19)	9748(7)	-1204(19)	83
H(95B)	8443(35)	9679(5)	-717(4)	83
H(95C)	8905(18)	9822(5)	-1183(20)	83
H(97)	5463(5)	11011(4)	1078(3)	32

H(98)	4517(5)	10878(4)	1623(3)	38
H(99)	4720(6)	11200(4)	2391(4)	48
H(100)	5873(6)	11611(4)	2625(3)	42
H(101)	6838(5)	11701(4)	2096(3)	34
H(103)	5676(5)	12246(4)	898(3)	35
H(104)	5412(5)	13254(5)	473(3)	48
H(105)	6387(6)	13949(4)	197(3)	43
H(106)	7611(6)	13656(4)	372(3)	39
H(107)	7871(6)	12644(4)	790(3)	38
H(109)	8047(5)	10519(4)	1483(3)	38
H(11A)	9206(25)	12645(16)	1007(4)	67
H(11B)	9943(5)	12275(27)	814(5)	67
H(11C)	9204(25)	11827(13)	901(7)	67
H(111)	9398(5)	11608(5)	2343(3)	49
H(112)	8752(6)	12631(5)	2139(3)	47
H(113)	7794(5)	12599(4)	1597(3)	33
H(114)	9031(6)	10553(5)	2006(3)	50
H(90A)	6020(5)	6273(4)	460(4)	65
H(90B)	6633(5)	5852(4)	752(4)	65
H(90C)	1408(7)	9845(4)	8828(4)	89
H(90D)	671(7)	9444(4)	8990(4)	89

Crystal data and structure refinement for 113

Table 1. Crystal data and structure refinement for **113**.

Identification code	92
Empirical formula	C40 H46 Cl2 N6 Ru
Formula weight	82.80
Temperature	273(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21/c
Unit cell dimensions	a = 19.3615(12) A alpha = 90 deg. b = 15.9432(8) A beta = 103.388(2) deg. c = 12.5846(6) A gamma = 90 deg.
Volume	3779.1(4) A^3
Z, Calculated density	4, 1.376 Mg/m^3
Absorption coefficient	0.593 mm^-1
F(000)	624
Crystal size	0.02 x 0.01 x 0.01 mm
Theta range for data collection	3.05 to 27.50 deg.
Limiting indices	-22<=h<=25, -17<=k<=20, -16<=l<=13
Reflections collected / unique	24492 / 8572 [R(int) = 0.1435]
Completeness to theta = 27.50	98.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9941 and 0.9882
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8572 / 0 / 443
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0790, wR2 = 0.1580
R indices (all data)	R1 = 0.1482, wR2 = 0.1973
Extinction coefficient	0.0017(4)
Largest diff. peak and hole	1.264 and -1.395 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2x 10^3) for s92. U(eq) is defined as one third of the trace of the orthogonalised Uij tensor.

	x	y	z	U(eq)
C(18)	1190(4)	3143(4)	8491(6)	41(2)
C(19)	1601(4)	2346(4)	8334(7)	51(2)
C(20)	452(4)	2885(5)	8665(8)	62(2)
C(21)	1796(4)	6048(4)	10152(6)	47(2)
C(22)	1211(5)	6341(5)	10696(8)	60(2)
C(23)	2499(4)	6505(5)	10646(7)	54(2)
C(34)	3743(4)	3167(4)	6101(7)	50(2)
C(35)	3639(5)	4002(5)	4383(6)	52(2)
C(40)	4009(4)	5017(5)	9440(7)	51(2)
C(1)	1233(3)	5196(4)	7525(5)	32(2)
C(2)	2589(3)	5741(4)	5657(5)	26(1)
C(3)	49(3)	5396(4)	7372(6)	39(2)
C(4)	308(4)	5076(4)	8338(7)	41(2)
C(5)	2487(4)	6388(4)	3996(5)	33(2)
C(6)	3168(4)	6183(4)	4382(5)	34(2)
C(7)	624(3)	5823(4)	5839(6)	32(2)
C(8)	62(4)	6128(4)	5054(6)	41(2)
C(9)	198(4)	6470(4)	4132(6)	44(2)
C(10)	887(4)	6509(4)	3976(6)	37(2)
C(11)	1413(3)	6160(4)	4779(5)	31(2)
C(12)	1511(4)	4580(4)	9393(6)	38(2)
C(13)	1872(4)	5094(4)	10232(6)	39(2)
C(14)	2281(5)	4709(5)	11144(6)	56(2)
C(15)	2331(5)	3829(5)	11235(7)	59(2)
C(16)	1974(4)	3339(5)	10382(6)	46(2)
C(17)	1561(4)	3690(4)	9434(5)	33(2)
C(24)	3908(3)	5565(4)	6099(5)	30(2)
C(25)	4345(3)	6204(4)	6624(5)	33(2)
C(26)	5003(4)	5961(4)	7282(6)	39(2)
C(27)	5207(4)	5138(4)	7401(6)	43(2)
C(28)	4763(3)	4526(4)	6863(6)	39(2)
C(29)	4106(3)	4708(4)	6192(5)	32(2)
C(30)	4127(4)	7123(4)	6505(6)	36(2)
C(31)	4112(4)	7518(4)	7604(6)	45(2)
C(32)	4617(4)	7617(4)	5950(6)	45(2)
C(33)	3608(4)	4038(4)	5584(6)	38(2)
C(36)	2977(4)	4028(4)	8258(6)	40(2)
C(37)	3495(4)	3675(5)	9075(7)	52(2)
C(38)	4037(4)	4180(5)	9651(7)	49(2)

C(39)	3453(3)	5342(4)	8613(6)	38(2)
N(1)	615(3)	5483(3)	6863(5)	33(1)
N(2)	1039(3)	4947(3)	8435(5)	35(1)
N(3)	1299(3)	5827(3)	5701(4)	27(1)
N(4)	2143(3)	6098(3)	4777(4)	28(1)
N(5)	3238(3)	5800(3)	5394(4)	26(1)
N(6)	2927(3)	4862(3)	8050(4)	33(1)
Cl(2)	1815(1)	3997(1)	5948(1)	32(1)
Cl(3)	2257(1)	6741(1)	7623(1)	32(1)
Ru(1)	2082(1)	5359(1)	6822(1)	24(1)

Table 3. Bond lengths [A] and angles [deg] for s92.

C(18)-C(17)	1.514(9)
C(18)-C(19)	1.536(10)
C(18)-C(20)	1.549(10)
C(21)-C(13)	1.529(10)
C(21)-C(22)	1.527(10)
C(21)-C(23)	1.542(10)
C(34)-C(33)	1.530(9)
C(35)-C(33)	1.527(10)
C(40)-C(38)	1.360(11)
C(40)-C(39)	1.411(10)
C(1)-N(2)	1.345(8)
C(1)-N(1)	1.367(8)
C(1)-Ru(1)	2.056(6)
C(2)-N(4)	1.362(8)
C(2)-N(5)	1.376(8)
C(2)-Ru(1)	2.037(6)
C(3)-C(4)	1.307(10)
C(3)-N(1)	1.400(8)
C(4)-N(2)	1.407(9)
C(5)-C(6)	1.337(9)
C(5)-N(4)	1.388(8)
C(6)-N(5)	1.391(8)
C(7)-N(3)	1.357(8)
C(7)-C(8)	1.378(9)
C(7)-N(1)	1.402(9)
C(8)-C(9)	1.362(10)
C(9)-C(10)	1.394(10)
C(10)-C(11)	1.376(9)
C(11)-N(3)	1.341(8)
C(11)-N(4)	1.416(8)
C(12)-C(13)	1.390(10)
C(12)-C(17)	1.422(9)
C(12)-N(2)	1.456(9)
C(13)-C(14)	1.378(11)
C(14)-C(15)	1.409(11)
C(15)-C(16)	1.377(11)
C(16)-C(17)	1.391(10)
C(24)-C(25)	1.389(9)
C(24)-C(29)	1.415(9)
C(24)-N(5)	1.441(8)
C(25)-C(26)	1.405(9)
C(25)-C(30)	1.522(9)
C(26)-C(27)	1.368(10)
C(27)-C(28)	1.372(10)
C(28)-C(29)	1.386(9)

C(29)-C(33)	1.521(9)
C(30)-C(31)	1.526(10)
C(30)-C(32)	1.522(9)
C(36)-N(6)	1.353(8)
C(36)-C(37)	1.380(10)
C(37)-C(38)	1.385(11)
C(39)-N(6)	1.339(8)
N(3)-Ru(1)	1.964(5)
N(6)-Ru(1)	2.126(5)
Cl(2)-Ru(1)	2.4363(15)
Cl(3)-Ru(1)	2.4134(15)
C(17)-C(18)-C(19)	114.3(6)
C(17)-C(18)-C(20)	109.2(6)
C(19)-C(18)-C(20)	108.7(6)
C(13)-C(21)-C(22)	110.2(6)
C(13)-C(21)-C(23)	112.4(7)
C(22)-C(21)-C(23)	110.6(6)
C(38)-C(40)-C(39)	119.5(7)
N(2)-C(1)-N(1)	103.9(5)
N(2)-C(1)-Ru(1)	144.3(5)
N(1)-C(1)-Ru(1)	111.7(4)
N(4)-C(2)-N(5)	102.6(5)
N(4)-C(2)-Ru(1)	113.0(4)
N(5)-C(2)-Ru(1)	144.4(5)
C(4)-C(3)-N(1)	106.9(6)
C(3)-C(4)-N(2)	107.5(6)
C(6)-C(5)-N(4)	104.9(6)
C(5)-C(6)-N(5)	108.6(6)
N(3)-C(7)-C(8)	122.0(7)
N(3)-C(7)-N(1)	109.7(5)
C(8)-C(7)-N(1)	128.4(6)
C(9)-C(8)-C(7)	118.4(7)
C(8)-C(9)-C(10)	121.2(7)
C(11)-C(10)-C(9)	116.6(7)
N(3)-C(11)-C(10)	123.6(6)
N(3)-C(11)-N(4)	109.8(5)
C(10)-C(11)-N(4)	126.5(6)
C(13)-C(12)-C(17)	122.8(7)
C(13)-C(12)-N(2)	120.1(6)
C(17)-C(12)-N(2)	117.1(6)
C(14)-C(13)-C(12)	117.5(7)
C(14)-C(13)-C(21)	121.7(7)
C(12)-C(13)-C(21)	120.8(7)
C(13)-C(14)-C(15)	121.8(7)
C(16)-C(15)-C(14)	119.2(8)
C(17)-C(16)-C(15)	121.7(7)
C(16)-C(17)-C(12)	117.0(6)
C(16)-C(17)-C(18)	121.0(6)
C(12)-C(17)-C(18)	122.1(6)
C(25)-C(24)-C(29)	123.1(6)

C(25)-C(24)-N(5)	117.6(6)
C(29)-C(24)-N(5)	119.3(5)
C(24)-C(25)-C(26)	116.5(6)
C(24)-C(25)-C(30)	122.4(6)
C(26)-C(25)-C(30)	121.1(6)
C(27)-C(26)-C(25)	121.9(6)
C(26)-C(27)-C(28)	119.8(7)
C(27)-C(28)-C(29)	122.2(7)
C(28)-C(29)-C(24)	116.5(6)
C(28)-C(29)-C(33)	123.0(6)
C(24)-C(29)-C(33)	120.5(6)
C(25)-C(30)-C(31)	111.8(6)
C(25)-C(30)-C(32)	110.8(6)
C(31)-C(30)-C(32)	110.3(6)
C(29)-C(33)-C(35)	111.0(6)
C(29)-C(33)-C(34)	113.4(6)
C(35)-C(33)-C(34)	110.1(6)
N(6)-C(36)-C(37)	123.6(7)
C(38)-C(37)-C(36)	118.9(7)
C(40)-C(38)-C(37)	118.5(7)
N(6)-C(39)-C(40)	122.6(7)
C(1)-N(1)-C(3)	110.8(6)
C(1)-N(1)-C(7)	119.6(5)
C(3)-N(1)-C(7)	129.5(6)
C(1)-N(2)-C(4)	110.8(6)
C(1)-N(2)-C(12)	125.4(5)
C(4)-N(2)-C(12)	123.8(6)
C(11)-N(3)-C(7)	118.0(5)
C(11)-N(3)-Ru(1)	121.2(4)
C(7)-N(3)-Ru(1)	120.8(4)
C(2)-N(4)-C(5)	113.4(5)
C(2)-N(4)-C(11)	118.2(5)
C(5)-N(4)-C(11)	128.4(5)
C(2)-N(5)-C(6)	110.5(5)
C(2)-N(5)-C(24)	125.2(5)
C(6)-N(5)-C(24)	124.1(5)
C(39)-N(6)-C(36)	116.5(6)
C(39)-N(6)-Ru(1)	122.3(4)
C(36)-N(6)-Ru(1)	121.1(4)
N(3)-Ru(1)-C(2)	77.9(2)
N(3)-Ru(1)-C(1)	78.2(2)
C(2)-Ru(1)-C(1)	156.0(3)
N(3)-Ru(1)-N(6)	179.3(2)
C(2)-Ru(1)-N(6)	102.5(2)
C(1)-Ru(1)-N(6)	101.4(2)
N(3)-Ru(1)-Cl(3)	87.92(15)
C(2)-Ru(1)-Cl(3)	89.06(17)
C(1)-Ru(1)-Cl(3)	89.15(17)
N(6)-Ru(1)-Cl(3)	91.56(15)
N(3)-Ru(1)-Cl(2)	88.07(15)

C(2)-Ru(1)-Cl(2)	91.59(17)
C(1)-Ru(1)-Cl(2)	88.53(18)
N(6)-Ru(1)-Cl(2)	92.44(15)
Cl(3)-Ru(1)-Cl(2)	175.71(6)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for s92.

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(18)	42(4)	32(4)	46(5)	5(3)	6(4)	-4(3)
C(19)	62(5)	33(4)	63(6)	3(4)	22(4)	2(4)
C(20)	51(5)	47(5)	90(7)	-10(5)	21(5)	-16(4)
C(21)	64(5)	37(4)	46(5)	-3(3)	26(4)	-13(4)
C(22)	65(6)	52(5)	76(7)	-9(4)	42(5)	-8(4)
C(23)	70(6)	35(4)	62(6)	-11(4)	29(5)	-20(4)
C(34)	46(5)	30(4)	75(6)	-2(4)	13(4)	-1(3)
C(35)	73(6)	37(4)	46(5)	-5(3)	15(4)	0(4)
C(40)	40(4)	47(5)	58(6)	-6(4)	-1(4)	-2(4)
C(1)	35(4)	23(3)	39(4)	-4(3)	13(3)	-7(3)
C(2)	34(4)	20(3)	23(3)	-2(2)	7(3)	3(3)
C(3)	17(3)	42(4)	58(5)	-11(4)	9(3)	-6(3)
C(4)	40(4)	36(4)	56(5)	-9(3)	25(4)	-5(3)
C(5)	44(4)	33(4)	21(4)	3(3)	5(3)	2(3)
C(6)	41(4)	31(3)	32(4)	2(3)	13(3)	-8(3)
C(7)	29(4)	20(3)	46(4)	-1(3)	4(3)	-2(3)
C(8)	28(4)	33(4)	54(5)	-7(3)	-3(3)	6(3)
C(9)	39(4)	36(4)	47(5)	-2(3)	-8(4)	7(3)
C(10)	37(4)	42(4)	26(4)	-2(3)	-3(3)	6(3)
C(11)	32(4)	26(3)	32(4)	-2(3)	1(3)	7(3)
C(12)	38(4)	44(4)	33(4)	0(3)	13(3)	-5(3)
C(13)	52(5)	37(4)	31(4)	-3(3)	15(4)	-12(3)
C(14)	82(6)	50(5)	36(5)	-8(4)	13(4)	-34(5)
C(15)	77(6)	57(5)	39(5)	13(4)	4(4)	-11(5)
C(16)	59(5)	37(4)	46(5)	4(3)	17(4)	-12(4)
C(17)	40(4)	30(3)	32(4)	1(3)	15(3)	-7(3)
C(24)	22(3)	38(4)	30(4)	1(3)	8(3)	-4(3)
C(25)	27(4)	42(4)	32(4)	1(3)	10(3)	-6(3)
C(26)	30(4)	42(4)	45(5)	-6(3)	8(3)	-11(3)
C(27)	27(4)	41(4)	58(5)	5(3)	2(3)	-3(3)
C(28)	25(4)	40(4)	48(5)	6(3)	2(3)	6(3)
C(29)	29(3)	32(3)	41(4)	0(3)	16(3)	2(3)
C(30)	31(4)	29(3)	46(4)	-3(3)	8(3)	-6(3)
C(31)	40(4)	34(4)	65(6)	-15(3)	19(4)	-15(3)
C(32)	60(5)	40(4)	39(5)	2(3)	21(4)	-6(4)
C(33)	29(4)	30(4)	52(5)	3(3)	5(3)	7(3)
C(36)	40(4)	31(4)	43(4)	6(3)	0(3)	2(3)

C(37)	51(5)	36(4)	59(6)	7(4)	-8(4)	-2(4)
C(38)	48(5)	47(5)	47(5)	4(4)	-3(4)	10(4)
C(39)	28(4)	38(4)	44(4)	-2(3)	1(3)	1(3)
N(1)	17(3)	31(3)	49(4)	-3(3)	6(2)	-2(2)
N(2)	33(3)	25(3)	53(4)	-4(2)	25(3)	-4(2)
N(3)	21(3)	24(3)	33(3)	-4(2)	1(2)	1(2)
N(4)	31(3)	27(3)	23(3)	1(2)	1(2)	0(2)
N(5)	22(3)	24(3)	32(3)	4(2)	9(2)	-4(2)
N(6)	29(3)	31(3)	36(3)	2(2)	0(3)	-2(2)
Cl(2)	27(1)	25(1)	43(1)	-6(1)	6(1)	0(1)
Cl(3)	37(1)	23(1)	37(1)	-3(1)	10(1)	-3(1)
Ru(1)	22(1)	22(1)	29(1)	0(1)	6(1)	-1(1)

Crystal data and structure refinement for **278**

Table 1. Crystal data and structure refinement for **278**

Identification code	05neo017	
Empirical formula	C12 H14 Cl1 N2 O2	
Formula weight	126.35	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P212121	
Unit cell dimensions	a = 7.9514(12) Å	a= 90°
	b = 10.6720(16) Å	b= 90°
	c = 14.8120(18) Å	g = 90°
Volume	1256.9(3) $Å^3$	
Z	8	
Density (calculated)	1.335 Mg/m^3	
Absorption coefficient	0.295 mm^{-1}	
F(000)	528	
Crystal size	0.15 x 0.10 x 0.05 mm^3	
Theta range for data collection	3.19 to 27.55°.	
Index ranges	-10<=h<=7, -13<=k<=13, -16<=l<=19	
Reflections collected	5493	
Independent reflections	2852 [R(int) = 0.0531]	
Completeness to theta = 27.55°	99.4 %	
Absorption correction	None	
Max. and min. transmission	0.9854 and 0.5298	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2852 / 0 / 155	
Goodness-of-fit on F^2	1.134	
Final R indices [I>2sigma(I)]	R1 = 0.1023, wR2 = 0.2786	
R indices (all data)	R1 = 0.1391, wR2 = 0.3093	
Absolute structure parameter	-1.7(2)	
Largest diff. peak and hole	0.807 and -0.747 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 05neo017. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	9545(2)	6508(1)	8875(1)	21(1)
O(2)	15728(11)	6522(7)	9590(5)	81(2)
C(7)	9395(11)	1979(8)	8828(6)	44(2)
N(1)	15265(10)	3998(6)	7114(5)	47(2)
C(2)	15300(13)	4940(8)	7761(6)	51(2)
C(12)	9141(12)	801(8)	9129(6)	51(2)
O(1)	12292(8)	1766(6)	8561(5)	57(2)
C(1)	13779(11)	3432(8)	7145(6)	47(2)
C(8)	7984(11)	2800(9)	8822(6)	53(2)
N(2)	12824(9)	4005(6)	7735(5)	43(2)
C(6)	11017(11)	2379(7)	8475(6)	43(2)
C(5)	11093(12)	3636(9)	7955(6)	51(2)
C(4)	16718(12)	3689(11)	6552(7)	61(3)
C(10)	6229(14)	1158(9)	9426(7)	57(3)
C(3)	13678(12)	4943(8)	8159(6)	49(2)
C(11)	7653(12)	350(9)	9451(6)	47(2)
C(9)	6382(12)	2316(10)	9120(6)	55(2)

Table 3. Bond lengths [Å] and angles [°] for 05neo017.

C(7)-C(12)	1.349(13)
C(7)-C(8)	1.424(12)
C(7)-C(6)	1.455(12)
N(1)-C(1)	1.328(11)
N(1)-C(2)	1.389(11)
N(1)-C(4)	1.462(11)
C(2)-C(3)	1.418(13)
C(2)-H(2)	0.9500
C(12)-C(11)	1.363(13)
C(12)-H(12)	0.9500
O(1)-C(6)	1.213(10)
C(1)-N(2)	1.310(11)
C(1)-H(1)	0.9500
C(8)-C(9)	1.444(13)
C(8)-H(8)	0.9500
N(2)-C(3)	1.363(11)
N(2)-C(5)	1.468(12)
C(6)-C(5)	1.548(12)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(4)-H(4C)	0.9800
C(10)-C(9)	1.322(14)
C(10)-C(11)	1.424(14)
C(10)-H(10)	0.9500
C(3)-H(3)	0.9500
C(11)-H(11)	0.9500
C(9)-H(9)	0.9500
C(12)-C(7)-C(8)	117.2(9)
C(12)-C(7)-C(6)	121.6(8)
C(8)-C(7)-C(6)	121.1(7)
C(1)-N(1)-C(2)	108.9(8)
C(1)-N(1)-C(4)	128.3(8)
C(2)-N(1)-C(4)	122.7(8)
N(1)-C(2)-C(3)	105.7(8)
N(1)-C(2)-H(2)	127.2
C(3)-C(2)-H(2)	127.2
C(7)-C(12)-C(11)	125.1(9)
C(7)-C(12)-H(12)	117.5
C(11)-C(12)-H(12)	117.5
N(2)-C(1)-N(1)	109.1(8)
N(2)-C(1)-H(1)	125.5
N(1)-C(1)-H(1)	125.5
C(7)-C(8)-C(9)	118.3(9)
C(7)-C(8)-H(8)	120.9
C(9)-C(8)-H(8)	120.9
C(1)-N(2)-C(3)	111.2(8)

C(1)-N(2)-C(5)	124.5(8)
C(3)-N(2)-C(5)	124.2(8)
O(1)-C(6)-C(7)	123.0(7)
O(1)-C(6)-C(5)	119.1(8)
C(7)-C(6)-C(5)	117.8(7)
N(2)-C(5)-C(6)	112.3(7)
N(2)-C(5)-H(5A)	109.1
C(6)-C(5)-H(5A)	109.1
N(2)-C(5)-H(5B)	109.1
C(6)-C(5)-H(5B)	109.1
H(5A)-C(5)-H(5B)	107.9
N(1)-C(4)-H(4A)	109.5
N(1)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	109.5
N(1)-C(4)-H(4C)	109.5
H(4A)-C(4)-H(4C)	109.5
H(4B)-C(4)-H(4C)	109.5
C(9)-C(10)-C(11)	120.1(10)
C(9)-C(10)-H(10)	119.9
C(11)-C(10)-H(10)	119.9
N(2)-C(3)-C(2)	105.1(8)
N(2)-C(3)-H(3)	127.5
C(2)-C(3)-H(3)	127.5
C(12)-C(11)-C(10)	117.9(8)
C(12)-C(11)-H(11)	121.1
C(10)-C(11)-H(11)	121.1
C(10)-C(9)-C(8)	121.3(10)
C(10)-C(9)-H(9)	119.3
C(8)-C(9)-H(9)	119.3

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 05neo017. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	21(1)	19(1)	23(1)	0(1)	2(1)	6(1)
O(2)	99(6)	70(4)	76(5)	-1(4)	9(4)	-45(5)
C(7)	40(4)	49(4)	43(4)	1(4)	-8(5)	2(4)
N(1)	50(4)	43(3)	49(4)	2(3)	8(4)	1(4)
C(2)	62(6)	35(4)	56(5)	5(4)	-5(5)	1(4)
C(12)	49(6)	48(5)	57(5)	3(4)	8(4)	1(4)
O(1)	42(3)	56(4)	75(4)	7(3)	9(3)	2(3)
C(1)	47(5)	39(4)	54(5)	-2(4)	-4(4)	6(4)
C(8)	48(5)	56(5)	55(5)	-3(5)	20(5)	11(4)
N(2)	54(4)	36(3)	38(3)	4(3)	9(3)	2(3)
C(6)	51(5)	32(4)	45(4)	0(3)	-4(4)	1(4)
C(5)	47(5)	60(5)	45(4)	-1(4)	4(4)	1(4)
C(4)	46(5)	76(7)	60(5)	-3(5)	10(5)	21(5)
C(10)	63(6)	50(5)	58(6)	2(4)	13(5)	-7(4)
C(3)	53(6)	42(4)	53(5)	6(4)	7(5)	-7(4)
C(11)	48(5)	51(5)	42(4)	9(4)	6(4)	0(4)
C(9)	45(5)	70(6)	50(5)	-5(4)	2(4)	1(5)

Crystal data and structure refinement for 286

Table 1. Crystal data and structure refinement for **286**

Identification code	05neo011	
Empirical formula	C24 H24 Ag2 Br2 N4 O2	
Formula weight	776.03	
Temperature	120(2) K	
Wavelength	71.073 pm	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 2567.8(11) pm	a= 90°
	b = 634.4(3) pm	b= 104.46(3)°
	c = 1635.5(4) pm	g = 90°
Volume	2.5799(18) nm^3	
Z	4	
Density (calculated)	1.998 Mg/m^3	
Absorption coefficient	4.644 mm^{-1}	
F(000)	1504	
Crystal size	0.04 x 0.02 x 0.01 mm^3	
Theta range for data collection	3.28 to 27.52°.	
Index ranges	-32<=h<=32, -8<=k<=8, -21<=l<=21	
Reflections collected	17751	
Independent reflections	2927 [R(int) = 0.0694]	
Completeness to theta = 27.52°	98.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9550 and 0.8360	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2927 / 0 / 156	
Goodness-of-fit on F^2	1.045	
Final R indices [I>2sigma(I)]	R1 = 0.0384, wR2 = 0.0713	
R indices (all data)	R1 = 0.0615, wR2 = 0.0786	
Largest diff. peak and hole	0.730 and -0.581 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for 05neo011. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Ag(1)	0	2194(1)	2500	19(1)
Ag(2)	0	-2718(1)	2500	28(1)
Br(1)	-983(1)	-2546(1)	2366(1)	28(1)
O(1)	1315(1)	5299(5)	4739(2)	31(1)
N(1)	558(1)	2140(5)	4431(2)	20(1)
N(2)	-300(1)	2522(5)	4210(2)	18(1)
C(11)	-89(2)	2572(6)	5077(2)	21(1)
C(10)	450(2)	2340(6)	5218(3)	23(1)
C(12)	-876(2)	2641(6)	3786(3)	23(1)
C(1)	89(2)	2264(6)	3804(2)	19(1)
C(5)	2105(2)	1860(7)	3724(3)	29(1)
C(4)	1945(2)	3656(7)	4092(2)	22(1)
C(9)	2266(2)	5476(7)	4177(3)	29(1)
C(8)	2736(2)	5502(8)	3906(3)	35(1)
C(7)	2894(2)	3705(8)	3540(3)	33(1)
C(6)	2579(2)	1886(8)	3454(3)	33(1)
C(2)	1086(2)	1776(6)	4272(3)	24(1)
C(3)	1440(2)	3732(7)	4397(2)	22(1)

Table 3. Bond lengths [pm] and angles [°] for 05neo011.

Ag(1)-C(1)#1	208.8(4)
Ag(1)-C(1)	208.8(4)
Ag(1)-Ag(2)	311.63(16)
Ag(1)-Ag(2)#2	322.77(17)
Ag(2)-Br(1)	248.05(12)
Ag(2)-Br(1)#1	248.05(12)
Ag(2)-Ag(1)#3	322.77(17)
O(1)-C(3)	122.3(5)
N(1)-C(1)	137.6(5)
N(1)-C(10)	138.8(5)
N(1)-C(2)	146.1(5)
N(2)-C(1)	134.1(5)
N(2)-C(11)	138.6(5)
N(2)-C(12)	147.1(5)
C(11)-C(10)	135.6(6)
C(11)-H(11)	95.00
C(10)-H(10)	95.00
C(12)-H(12A)	98.00
C(12)-H(12B)	98.00
C(12)-H(12C)	98.00
C(5)-C(6)	139.5(6)
C(5)-C(4)	139.7(6)
C(5)-H(5)	95.00
C(4)-C(9)	140.5(6)
C(4)-C(3)	150.3(6)
C(9)-C(8)	138.6(6)
C(9)-H(9)	95.00
C(8)-C(7)	139.4(7)
C(8)-H(8)	95.00
C(7)-C(6)	139.7(7)
C(7)-H(7)	95.00
C(6)-H(6)	95.00
C(2)-C(3)	152.2(6)
C(2)-H(2A)	99.00
C(2)-H(2B)	99.00
C(1)#1-Ag(1)-C(1)	177.6(2)
C(1)#1-Ag(1)-Ag(2)	91.22(10)
C(1)-Ag(1)-Ag(2)	91.22(10)
C(1)#1-Ag(1)-Ag(2)#2	88.78(10)
C(1)-Ag(1)-Ag(2)#2	88.78(10)
Ag(2)-Ag(1)-Ag(2)#2	180.0
Br(1)-Ag(2)-Br(1)#1	174.94(3)
Br(1)-Ag(2)-Ag(1)	87.471(15)
Br(1)#1-Ag(2)-Ag(1)	87.471(15)
Br(1)-Ag(2)-Ag(1)#3	92.529(15)
Br(1)#1-Ag(2)-Ag(1)#3	92.529(15)
Ag(1)-Ag(2)-Ag(1)#3	180.0

C(1)-N(1)-C(10)	110.3(3)
C(1)-N(1)-C(2)	123.7(3)
C(10)-N(1)-C(2)	126.0(3)
C(1)-N(2)-C(11)	111.2(3)
C(1)-N(2)-C(12)	124.0(3)
C(11)-N(2)-C(12)	124.8(3)
C(10)-C(11)-N(2)	107.1(3)
C(10)-C(11)-H(11)	126.5
N(2)-C(11)-H(11)	126.5
C(11)-C(10)-N(1)	106.4(3)
C(11)-C(10)-H(10)	126.8
N(1)-C(10)-H(10)	126.8
N(2)-C(12)-H(12A)	109.5
N(2)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
N(2)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
N(2)-C(1)-N(1)	105.0(3)
N(2)-C(1)-Ag(1)	127.2(3)
N(1)-C(1)-Ag(1)	127.8(3)
C(6)-C(5)-C(4)	120.0(4)
C(6)-C(5)-H(5)	120.0
C(4)-C(5)-H(5)	120.0
C(5)-C(4)-C(9)	119.0(4)
C(5)-C(4)-C(3)	122.6(4)
C(9)-C(4)-C(3)	118.3(4)
C(8)-C(9)-C(4)	120.9(5)
C(8)-C(9)-H(9)	119.5
C(4)-C(9)-H(9)	119.5
C(9)-C(8)-C(7)	119.9(5)
C(9)-C(8)-H(8)	120.1
C(7)-C(8)-H(8)	120.1
C(8)-C(7)-C(6)	119.6(4)
C(8)-C(7)-H(7)	120.2
C(6)-C(7)-H(7)	120.2
C(5)-C(6)-C(7)	120.5(4)
C(5)-C(6)-H(6)	119.7
C(7)-C(6)-H(6)	119.7
N(1)-C(2)-C(3)	113.4(3)
N(1)-C(2)-H(2A)	108.9
C(3)-C(2)-H(2A)	108.9
N(1)-C(2)-H(2B)	108.9
C(3)-C(2)-H(2B)	108.9
H(2A)-C(2)-H(2B)	107.7
O(1)-C(3)-C(4)	121.7(4)
O(1)-C(3)-C(2)	120.5(4)
C(4)-C(3)-C(2)	117.8(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$)for 05neo011. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Ag(1)	22(1)	21(1)	15(1)	0	7(1)	0
Ag(2)	27(1)	30(1)	25(1)	0	7(1)	0
Br(1)	27(1)	29(1)	27(1)	3(1)	6(1)	0(1)
O(1)	35(2)	27(2)	36(2)	-11(1)	16(2)	-8(1)
N(1)	21(2)	19(2)	20(2)	-2(1)	6(1)	-3(1)
N(2)	21(2)	19(2)	17(2)	0(1)	8(1)	-3(1)
C(11)	30(2)	20(2)	16(2)	-2(2)	10(2)	-6(2)
C(10)	34(3)	16(2)	17(2)	-1(2)	4(2)	-2(2)
C(12)	20(2)	27(2)	23(2)	0(2)	6(2)	-1(2)
C(1)	23(2)	18(2)	14(2)	-2(2)	4(2)	-3(2)
C(5)	29(3)	30(3)	25(2)	-3(2)	1(2)	2(2)
C(4)	17(2)	29(2)	17(2)	2(2)	2(2)	1(2)
C(9)	22(3)	30(2)	36(3)	-6(2)	8(2)	0(2)
C(8)	26(3)	37(3)	45(3)	4(2)	12(2)	-6(2)
C(7)	21(3)	50(3)	28(3)	5(2)	8(2)	4(2)
C(6)	29(3)	39(3)	31(3)	-3(2)	11(2)	9(2)
C(2)	25(2)	22(2)	24(2)	-3(2)	3(2)	0(2)
C(3)	23(3)	24(2)	15(2)	0(2)	-2(2)	0(2)

Chapter 11

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